Photoinduced, Copper-Catalyzed Alkylation of Amides with Unactivated Secondary Alkyl Halides at Room Temperature

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Supporting Information

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I. General Information

The following reagents were purchased and used as received:

Aldrich: CuI (99.999%; 98% and 99.5% provide comparable results), 1-adamantanecarboxamide, cyclohexanecarboxamide, 2-oxazolidinone, pivalamide, 2-bromoadamantane, bromocyclohexane, bromocycloheptane, 1-bromo-2,2-dimethylpropane, *t*-butyl 4-bromopiperidine-1-carboxylate, 4-bromotetrahydro-2*H*-pyran, and iodocyclohexane.

Alfa: LiO*t*-Bu, benzamide, 4-cyanobenzamide, 4-fluorobenzamide, 4-methoxybenzamide, 1-naphthamide, 2-naphthamide, thiophene-2-carboxamide, and 4-bromoheptane.

Eastman: furan-2-carboxamide.

Oakwood: 2-phenylacetamide.

Matrix: 4-(trifluoromethyl)benzamide.

Maybridge: *t*-butyl 4-carbamoylpiperidine-1-carboxylate

TCI: nicotinamide, *n*-octanamide.

DMF and CH_3CN were dried in a solvent-purification system with the aid of activated alumina.

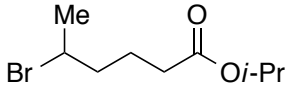
All reactions were carried out in oven-dried quartz tubes or quartz flasks under an inert atmosphere using a Luzchem LZC–4V photoreactor at 254 nm.

^{1}H and ^{13}C NMR data were collected on a VARIAN 500 MHz spectrometer at ambient temperature. GC analyses were carried out on an Agilent 6890 series system with a DB-1 column (length 30 m, i.d. 0.25 mm) and an Agilent 6850 series system with a G-TA column (length 30 m, i.d. 0.25 mm). GC-MS analyses were performed on an Agilent 6980 series system equipped with an Agilent 5973 Network Mass Selective Detector.

II. Preparation of Materials

These procedures have not been optimized.

General procedure for the preparation of alkyl bromides. A 300-mL round-bottom flask was charged with PPh_3 (17.0 g, 65.0 mmol, 1.30 equiv), imidazole (4.42 g, 65.0 mmol, 1.30 equiv), and dichloromethane (150 mL). The resulting solution was stirred at 0 °C in an ice bath under a nitrogen atmosphere. Bromine (3.40 mL, 65.0 mmol, 1.30 equiv) was added dropwise over 2 min, yielding a colorless or light-yellow solution. After 5 min, the alcohol (50.0 mmol, 1.00 equiv) was added dropwise over 3 min. The ice bath was then removed, and the reaction mixture was stirred at room temperature for 20 h. Next, the reaction mixture was concentrated under reduced pressure on a rotary evaporator to a volume of 40 mL, and then it was diluted with a mixture of pentane and ether (4/1, 100 mL). The resulting suspension was filtered and concentrated, and then the residue was purified by column chromatography.



Isopropyl 5-bromohexanoate. The title compound was prepared according to the general procedure, using isopropyl 5-hydroxyhexanoate.[1] The product was obtained as a colorless oil (8.53 g, 72% yield).

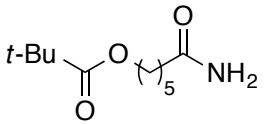
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.00 (hept, J = 6.3 Hz, 1H), 4.17 – 4.07 (m, 1H), 2.34 – 2.24 (m, 2H), 1.91 – 1.67 (m, 7H), 1.23 (d, J = 6.3 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 67.6, 50.8, 40.3, 33.8, 26.4, 23.2, 21.8.

FT-IR (neat) 2980, 2935, 1728, 1454, 1373, 1253, 1182, 1107 cm^{-1}.

MS (EI) *m*/*z* ($[M - C_3H_7O]^+$) calcd for $C_6H_{10}BrO$: 177.0, found: 177.1.

Preparation of amides.



6-Amino-6-oxohexyl pivalate. The title compound was prepared according to a reported procedure[2] from 6-hydroxyhexanamide.[3] The product was obtained as a white solid (61% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.85 (br s, 1H), 5.59 (br s, 1H), 4.04 (t, J = 6.6 Hz, 2H), 2.22 (t, J = 7.5 Hz, 2H), 1.73 – 1.57 (m, 4H), 1.44 – 1.34 (m, 2H), 1.17 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.6, 175.4, 64.1, 38.7, 35.7, 28.4, 27.2, 25.5, 25.0.

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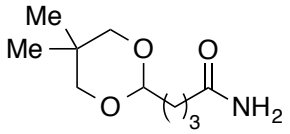
(1) Nemoto, H.; Zhong, W.; Kawamura T.; Kamiya, M.; Nakano, Y.; Sakamoto, K. *Synlett* **2007**, 2343–2346.

(2) Miranda, M. O.; Pietrangelo, A.; Hillmyer, M. A.; Tolman, W. B. *Green Chem.* **2012**, *14*, 490–494.

(3) Zhou, J.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 12527–12530.

FT-IR (neat) 3346, 3172, 2970, 2947, 2869, 2812, 1718, 1667, 1629, 1476, 1413, 1395, 1352, 1284, 1176, 1156, 1062, 1032, 953 cm^{-1}.

MS (EI) *m*/*z* ([M – C_4H_9]$^+$) calcd for $C_7H_{12}NO_3$: 158.1, found: 158.0.



4-(5,5-Dimethyl-1,3-dioxan-2-yl)butanamide. The title compound was prepared according to a reported procedure[4] from methyl 4-(5,5-dimethyl-1,3-dioxan-2-yl)butanoate.[5] The product was obtained as a white solid (65% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 (br s, 1H), 5.67 (br s, 1H), 4.43 (t, J = 4.8 Hz, 1H), 3.58 (dt, J = 11.2, 1.4 Hz, 2H), 3.46 – 3.36 (m, 2H), 2.26 (t, J = 7.4 Hz, 2H), 1.84 – 1.62 (m, 4H), 1.16 (s, 3H), 0.70 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 101.8, 77.2, 35.6, 33.8, 30.1, 23.0, 21.8, 20.0.

FT-IR (neat) 3387, 3304, 3195, 2966, 2955, 2903, 2872, 2843, 1657, 1631, 1466, 1410, 1346, 1318, 1240, 1216, 1176, 1127, 1097, 1075, 1020, 965, 925, 915, 818, 791 cm^{-1}.

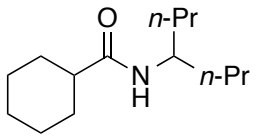
MS (EI) *m*/*z* (M^+) calcd for $C_{10}H_{19}NO_3$: 201.1, found: 201.2.

III. Photoinduced, Copper-Catalyzed Alkylations of Amides

General procedure for the alkylation of amides. CuI (19.5 mg, 0.10 mmol), the amide (1.00 mmol), and LiO*t*-Bu (160 mg, 2.00 mmol) were added to an oven-dried 10-mL quartz test tube that contained a stir bar (3 mm x 13 mm). The test tube was fitted with a rubber septum, the joint was wrapped with electrical tape, and the test tube was evacuated and backfilled with nitrogen (3 cycles). A solution of the alkyl bromide (2.00 mmol) in CH_3CN (5.4 mL) and DMF (0.80 mL) was added in turn by syringe. The test tube was detached from the nitrogen line, and the puncture holes of the septum were covered with vacuum grease. The resulting mixture was stirred vigorously for 5 min, and then the quartz test tube was placed in a Luzchem photoreactor. The stirring mixture was irradiated with a UVC lamp centered at 254 nm for 24 h. During the first 12 h, the reaction tube was occasionally shaken vertically (every 2-3 h) to ensure good mixing of the entire reaction mixture. After 24 h, the reaction mixture was purified by column chromatography.

(4) Bundesmann, M. W.; Coffey, S. B.; Wright, S. W. *Tetrahedron Lett.* **2010**, *51*, 3879–3882.

(5) The ester was synthesized from 4-(5,5-dimethyl-1,3-dioxan-2-yl)butanal (Alfa) using a literature method: Maki, B. E.; Scheidt, K. A. *Org. Lett.* **2008**, *10*, 4331–4334.



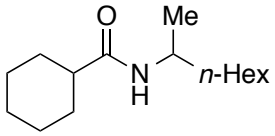
***N*-(Heptan-4-yl)cyclohexanecarboxamide (Table 2, Entry 1).** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and 4-bromoheptane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 148 mg (66%). Second run: 144 mg (64%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.08 (d, J = 8.9 Hz, 1H), 3.99 – 3.87 (m, 1H), 2.04 (tt, J = 11.7, 3.5 Hz, 1H), 1.88 – 1.62 (m, 6H), 1.49 – 1.18 (m, 12H), 0.89 (t, J = 7.1 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 48.3, 45.9, 37.7, 29.9, 25.78, 25.77, 19.1, 14.1.

FT-IR (neat) 3276, 3084, 2956, 2931, 2873, 2852, 1635, 1553, 1466, 1457, 1441, 1390, 1333, 1258, 1216, 1165, 1120, 948, 897, 763, 737, 709 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{14}H_{27}NO$: 225.2, found: 225.3.



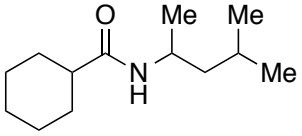
***N*-(Octan-2-yl)cyclohexanecarboxamide (Table 2, Entry 2).** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and 2-bromooctane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 202 mg (84%). Second run: 207 mg (86%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.18 (d, J = 8.6 Hz, 1H), 4.01 – 3.91 (m, 1H), 2.02 (tt, J = 11.8, 3.5 Hz, 1H), 1.88 – 1.62 (m, 5H), 1.48 – 1.15 (m, 15H), 1.10 (d, J = 6.6 Hz, 3H), 0.93 – 0.82 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 175.3, 45.8, 44.7, 37.1, 31.8, 29.9, 29.7, 29.2, 26.0, 25.79, 25.76, 25.75, 22.6, 21.1, 14.1.

FT-IR (neat) 3286, 3079, 2973, 2924, 2851, 1638, 1546, 1464, 1444, 1381, 1260, 1215, 1162, 1124, 957, 931, 895, 701 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{15}H_{29}NO$: 239.2, found: 239.3.



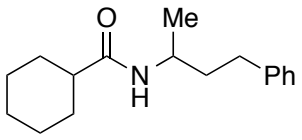
***N*-(4-Methylpentan-2-yl)cyclohexanecarboxamide (Table 2, Entry 3).** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and 2-bromo-4-methylpentane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 171 mg (81%). Second run: 176 mg (83%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.15 (d, J = 8.6 Hz, 1H), 4.10 – 4.00 (m, 1H), 2.01 (tt, J = 11.8, 3.5 Hz, 1H), 1.88 – 1.52 (m, 6H), 1.48 – 1.13 (m, 7H), 1.09 (d, J = 6.5 Hz, 3H), 0.90 (dd, J = 6.6, 2.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 46.5, 45.8, 43.0, 29.9, 29.6, 25.79, 25.76, 25.74, 25.1, 22.8, 22.5, 21.6.

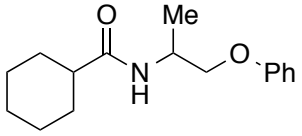
FT-IR (neat) 3289, 3071, 2964, 2928, 2852, 1632, 1541, 1442, 1383, 1259, 1213, 1165, 1127, 953, 896, 697 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{13}H_{25}NO$: 211.2, found: 211.3.



***N*-(4-Phenylbutan-2-yl)cyclohexanecarboxamide (Table 2, Entry 4) [545360-34-7].** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and (3-bromobutyl)benzene (2.0 mmol). The product was purified by column chromatograpy (hexanes → 30% EtOAc/hexanes). Beige solid. First run: 192 mg (74%). Second run: 197 mg (76%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2H), 7.21 – 7.15 (m, 3H), 5.19 (d, J = 8.5, 1H), 4.11 – 4.02 (m, 1H), 2.64 (dd, J = 9.4, 6.7 Hz, 2H), 2.00 (tt, J = 11.8, 3.4 Hz, 1H), 1.87 – 1.58 (m, 7H), 1.47 – 1.35 (m, 2H), 1.31 – 1.18 (m, 3H), 1.16 (d, J = 6.6 Hz, 3H).



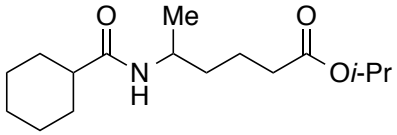
***N*-(1-Phenoxypropan-2-yl)cyclohexanecarboxamide (Table 2, Entry 5).** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and (2-bromopropoxy)benzene (2.0 mmol). The product was purified by column chromatography (20% EtOAc/hexanes → 50% EtOAc/hexanes). Off-white solid. First run: 163 mg (62%). Second run: 166 mg (64%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 6.96 (tt, J = 7.4, 1.1 Hz, 1H), 6.93 – 6.90 (m, 2H), 5.70 (d, J = 8.3 Hz, 1H), 4.42 – 4.34 (m, 1H), 3.99 – 3.90 (m, 2H), 2.06 (tt, J = 11.8, 3.5 Hz, 1H), 1.89 – 1.74 (m, 4H), 1.69 – 1.63 (m, 1H), 1.48 – 1.38 (m, 2H), 1.30 (d, J = 6.8 Hz, 3H), 1.28 – 1.20 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 175.6, 158.7, 129.5, 121.0, 114.5, 70.5, 45.6, 44.1, 29.6, 27.2, 25.7, 17.7.

FT-IR (neat) 3307, 2930, 2919, 2852, 1636, 1533 cm^{-1}.

MS (ESI) *m*/*z* $(M + H)^+$ calcd for $C_{16}H_{24}NO_2$: 262.2, found: 262.2.



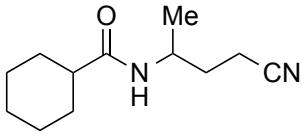
Isopropyl 5-(cyclohexanecarboxamido)hexanoate (Table 2, Entry 6). The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and isopropyl 5-bromohexanoate (2.0 mmol). The product was purified by column chromatography (hexanes → 50% EtOAc/hexanes). Light-tan solid. First run: 110 mg (39%). Second run: 104 mg (37%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.27 (d, J = 8.5 Hz, 1H), 4.99 (hept, J = 6.3 Hz, 1H), 4.04 – 3.92 (m, 1H), 2.36 – 2.19 (m, 2H), 2.02 (tt, J = 11.8, 3.5 Hz, 1H), 1.92 – 1.69 (m, 4H), 1.70 – 1.53 (m, 3H), 1.51 – 1.35 (m, 4H), 1.34 – 1.13 (m, 3H), 1.22 (d, J = 6.1 Hz, 6H), 1.11 (d, J = 6.6 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 173.1, 67.5, 45.7, 44.5, 36.2, 34.2, 29.8, 29.6, 25.76, 25.74, 25.73, 21.8, 21.4, 21.1.

FT-IR (neat) 3277, 3087, 2960, 2928, 2853, 1725, 1634, 1553, 1450, 1417, 1379, 1340, 1259, 1249, 1218, 1191, 1114, 957, 934, 895, 710 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{16}H_{29}NO_3$: 283.2, found: 283.3.



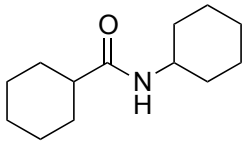
***N*-(4-Cyanobutan-2-yl)cyclohexanecarboxamide (Table 2, Entry 7).** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol), 4-bromopentanenitrile (2.0 mmol). The product was purified by column chromatography (20% EtOAc/hexanes → 50% EtOAc/hexanes). Beige solid. First run: 115 mg (55%). Second run: 116 mg (56%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.26 (d, J = 8.5 Hz, 1H), 4.13 – 4.08 (m, 1H), 2.43 – 2.31 (m, 2H), 2.06 (tt, J = 11.8, 3.5 Hz, 1H), 1.93 – 1.55 (m, 7H), 1.49 – 1.37 (m, 2H), 1.31 – 1.21 (m, 3H), 1.19 (d, J = 6.7 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1, 119.8, 45.5, 44.2, 32.7, 29.7, 29.6, 25.7, 20.8, 14.2.

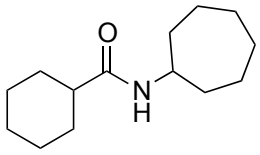
FT-IR (neat) 3295, 2974, 2931, 2852, 1637, 1541, 1443, 1428, 1390, 1376, 1261, 1217 cm^{-1}.

MS (ESI) *m*/*z* ($M + H)^+$ calcd for $C_{12}H_{21}N_2O$: 209.2, found: 209.2.



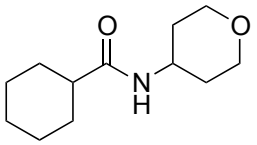
***N*-Cyclohexylcyclohexanecarboxamide (Table 2, Entry 8) [7474-36-4].** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and bromocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 180 mg (86%). Second run: 189 mg (90%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.31 (br s, 1H), 3.80 – 3.71 (m, 1H), 2.02 (tt, J = 11.8, 3.5 Hz, 1H), 1.98 – 1.56 (m, 9H), 1.46 – 1.04 (m, 11H).



***N*-Cycloheptylcyclohexanecarboxamide (Table 2, Entry 9) [550306-49-5].** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and bromocycloheptane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 131 mg (59%). Second run: 128 mg (57%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.40 (d, J = 8.3 Hz, 1H), 3.99 – 3.87 (m, 1H), 2.02 (tt, J = 11.8, 3.5 Hz, 1H), 1.94 – 1.14 (m, 22H).



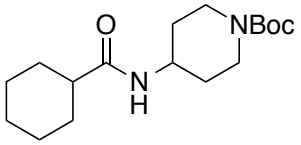
***N*-(Tetrahydro-2*H*-pyran-4-yl)cyclohexanecarboxamide (Table 2, Entry 10).** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and 4-bromotetrahydro-2*H*-pyran (2.0 mmol). The product was purified by column chromatography (hexanes → 50% EtOAc/hexanes). White solid. First run: 191 mg (90%). Second run: 194 mg (92%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.34 (d, J = 8.0 Hz, 1H), 4.04 – 3.90 (m, 3H), 3.47 (td, J = 11.7, 2.2 Hz, 2H), 2.03 (tt, J = 11.8, 3.5 Hz, 1H), 1.92 – 1.62 (m, 7H), 1.49 – 1.15 (m, 7H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 66.8, 45.6, 45.3, 33.3, 29.7, 25.7.

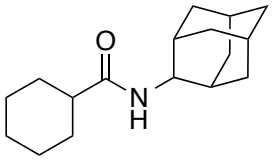
FT-IR (neat) 3250, 3072, 2969, 2928, 2851, 2832, 1627, 1549, 1446, 1389, 1364, 1335, 1236, 1216, 1142, 1133, 1012, 978, 953, 896, 847, 826, 691 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{12}H_{21}NO_2$: 211.2, found: 211.2.



***t*-Butyl 4-(cyclohexanecarboxamido)piperidine-1-carboxylate (Table 2, Entry 11) [1233955-27-5].** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and *t*-butyl 4-bromopiperidine-1-carboxylate (2.0 mmol). The product was purified by column chromatography (5% EtOAc/hexanes → 50% EtOAc/hexanes). Off-white solid. First run: 275 mg (89%). Second run: 284 mg (92%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.27 (d, J = 8.0 Hz, 1H), 4.03 (br s, 2H), 3.97 – 3.87 (m, 1H), 2.91 – 2.79 (m, 2H), 2.03 (tt, J = 11.8, 3.4 Hz, 1H), 1.93 – 1.63 (m, 7H), 1.46 (s, 9H), 1.44 – 1.38 (m, 2H), 1.32 – 1.21 (m, 5H).



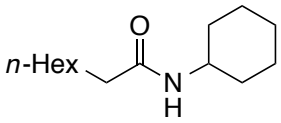
***N*-(Adamantan-2-yl)cyclohexanecarboxamide (Table 2, Entry 12).** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and 2-bromoadamantane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 196 mg (75%). Second run: 189 mg (72%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.76 (d, J = 8.0 Hz, 1H), 4.03 (dd, J = 7.6, 3.6 Hz, 1H), 2.08 (tt, J = 11.7, 3.5 Hz, 1H), 1.92 – 1.61 (m, 19H), 1.49 – 1.37 (m, 2H), 1.36 – 1.16 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 52.7, 45.8, 37.5, 37.1, 32.0, 31.9, 29.9, 27.2, 27.1, 25.8.

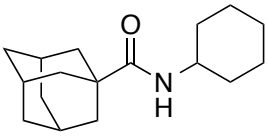
FT-IR (neat) 3324, 2906, 2850, 1733, 1640, 1538, 1471, 1444, 1387, 1310, 1252, 1211, 1179, 1141, 1110, 952, 894, 819, 668, 635 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{17}H_{27}NO$: 261.2, found: 261.3.



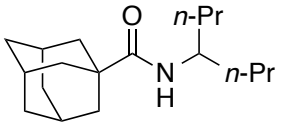
***N*-Cyclohexyloctanamide (Table 3, Entry 1) [42577-04-8].** The title compound was prepared according to the general procedure from *n*-octanamide (1.0 mmol) and bromocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 30% EtOAc/hexanes). White solid. First run: 194 mg (86%). Second run: 191 mg (85%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.44 (br s, 1H), 3.83 – 3.70 (m, 1H), 2.18 – 2.11 (m, 2H), 1.95 – 1.86 (m, 2H), 1.75 – 1.57 (m, 6H), 1.43 – 1.05 (m, 12H), 0.91 – 0.83 (m, 3H).



***N*-Cyclohexyl-1-adamantanecarboxamide (Table 3, Entry 2) [81311-58-2].** The title compound was prepared according to the general procedure from 1-adamantanecarboxamide (1.0 mmol) and bromocyclohexane (2.0 mmol). The product was purified by column chromatography (10% EtOAc/hexanes → 20% EtOAc/hexanes). Beige solid. First run: 220 mg (84%). Second run: 237 mg (91%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.41 (br s, 1H), 3.81 – 3.71 (m, 1H), 2.04 (s, 3H), 1.91 – 1.85 (m, 2H), 1.83 (d, J = 2.8 Hz, 6H), 1.77 – 1.65 (m, 9H), 1.43 – 1.32 (m, 2H), 1.22 – 1.05 (m, 3H).



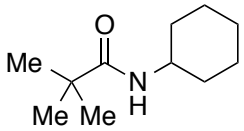
***N*-(Heptan-4-yl)-1-adamantanecarboxamide (Table 3, Entry 3).** The title compound was prepared according to the general procedure from 1-adamantanecarboxamide (1.0 mmol) and 4-bromoheptane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 173 mg (62%). Second run: 170 mg (61%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.22 (br s, 1H), 3.94 (br s, 1H), 2.09 – 2.00 (m, 3H), 1.90 –1.65 (m, 12H), 1.51 – 1.23 (m, 8H), 0.90 (t, J = 6.8 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 177.4, 48.2, 48.1, 40.6, 39.4, 37.7, 36.6, 28.2, 19.1, 14.1.

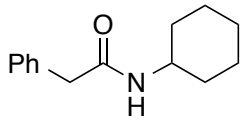
FT-IR (neat) 3296, 3076, 2957, 2927, 2916, 2901, 2890, 2871, 2850, 1626, 1544, 1447, 1368, 1343, 1285, 1272, 1140, 683 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{18}H_{31}NO$: 277.2, found: 277.3.



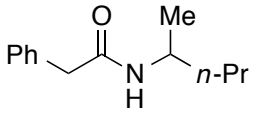
***N*-Cyclohexylpivalamide (Table 3, Entry 4) [4916-82-9].** The title compound was prepared according to the general procedure from pivalamide (1.0 mmol) and bromocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). Beige solid. First run: 165 mg (90%). Second run: 161 mg (88%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.44 (br s, 1H), 3.79 – 3.69 (m, 1H), 1.93 – 1.85 (m, 2H), 1.73 – 1.65 (m, 2H), 1.64 – 1.60 (m, 1H), 1.44 – 1.31 (m, 2H), 1.18 (s, 9H), 1.16 – 1.04 (m, 3H).



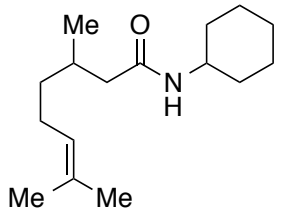
***N*-Cyclohexyl-2-phenylacetamide (Table 3, Entry 5) [10264-08-1].** The title compound was prepared according to the general procedure from 2-phenylacetamide (1.0 mmol) and bromocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 192 mg (88%). Second run: 201 mg (93%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.20 (m, 5H), 5.23 (br s, 1H), 3.80 – 3.71 (m, 1H), 3.55 (s, 2H), 1.90 – 1.49 (m, 5H), 1.39 – 1.26 (m, 2H), 1.18 – 0.95 (m, 3H).



***N*-(Pentan-2-yl)-2-phenylacetamide (Table 3, Entry 6) [304458-37-5].** The title compound was prepared according to the general procedure from 2-phenylacetamide (1.0 mmol) and 2-bromopentane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 155 mg (76%). Second run: 153 mg (75%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.22 (m, 5H), 5.14 (br s, 1H), 4.02 – 3.92 (m, 1H), 3.56 (d, J = 1.4 Hz, 2H), 1.37 – 1.16 (m, 4H), 1.04 (d, J = 6.6 Hz, 3H), 0.86 (t, J = 7.2 Hz, 3H).



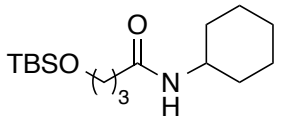
***N*-Cyclohexyl-3,7-dimethyloct-6-enamide (Table 3, Entry 7).** The title compound was prepared according to the general procedure from 3,7-dimethyloct-6-enamide (1.0 mmol) and bromocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). Light-tan solid. First run: 216 mg (86%). Second run: 222 mg (88%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.28 (d, J = 8.4 Hz, 1H), 5.11 – 5.06 (m, 1H), 3.83 – 3.73 (m, 1H), 2.16 (dd, J = 13.3, 5.7 Hz, 1H), 2.06 – 1.82 (m, 4H), 1.74 – 1.56 (m, 11H), 1.44 – 1.27 (m, 3H), 1.30 – 1.04 (m, 4H), 0.93 (d, J = 6.5 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 131.5, 124.4, 48.0, 44.8, 36.9, 33.3, 30.5, 25.7, 25.5, 25.4, 24.9, 19.5, 17.7.

FT-IR (neat) 3292, 3079, 2929, 2853, 1634, 1546, 1446, 1376, 1359, 1308, 1250, 1153, 1101, 989, 891, 723, 626 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{16}H_{29}NO$: 251.2, found: 251.3.



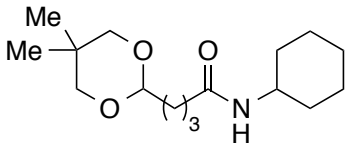
4-((*t*-Butyldimethylsilyl)oxy)-*N*-cyclohexylbutanamide (Table 3, Entry 8). The title compound was prepared according to the general procedure from 4-((*t*-butyldimethylsilyl)oxy)butanamide (1.0 mmol) and bromocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). Light-tan solid. First run: 245 mg (82%). Second run: 255 mg (85%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.45 (d, J = 8.1 Hz, 1H), 3.80 – 3.72 (m, 1H), 3.64 (t, J = 6.0 Hz, 2H), 2.23 (t, J = 7.4 Hz, 2H), 1.95 – 1.78 (m, 4H), 1.74 – 1.65 (m, 2H), 1.64 – 1.57 (m, 1H), 1.42 – 1.31 (m, 2H), 1.21 – 1.04 (m, 3H), 0.90 (s, 9H), 0.05 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.8, 62.1, 48.0, 33.27, 33.25, 28.6, 26.0, 25.6, 24.9, 18.3, –5.3.

FT-IR (neat) 3298, 3081, 2927, 2898, 2854, 1635, 1554, 1472, 1461, 1440, 1385, 1254, 1091, 1066, 991, 963, 879, 772, 723, 613 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{16}H_{33}NO_2Si$: 299.2, found: 299.3.



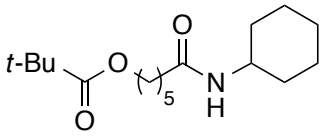
***N*-Cyclohexyl-4-(5,5-dimethyl-1,3-dioxan-2-yl)butanamide (Table 3, Entry 9).** The title compound was prepared according to the general procedure from 4-(5,5-dimethyl-1,3-dioxan-2-yl)butanamide (1.0 mmol) and bromocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 60% EtOAc/hexanes). Light-tan solid. First run: 251 mg (89%). Second run: 255 mg (90%).

^1H NMR (500 MHz, $CDCl_3$) δ 5.53 (d, J = 9.1 Hz, 1H), 4.42 (t, J = 4.8 Hz, 1H), 3.79 – 3.70 (m, 1H), 3.60 – 3.55 (m, 2H), 3.46 – 3.37 (m, 2H), 2.17 (t, J = 7.4 Hz, 2H), 1.93 – 1.54 (m, 9H), 1.40 – 1.28 (m, 2H), 1.22 – 1.03 (m, 3H), 1.17 (s, 3H), 0.71 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.7, 102.0, 77.2, 47.9, 36.6, 33.8, 33.2, 30.1, 25.6, 24.8, 23.0, 21.8, 20.4.

FT-IR (neat) 3254, 3074, 2932, 2855, 1630, 1550, 1473, 1448, 1396, 1363, 1176, 1133, 1112, 1090, 1026, 1012, 923, 870, 679 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{16}H_{29}NO_3$: 283.2, found: 283.3.



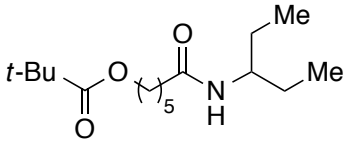
6-(Cyclohexylamino)-6-oxohexyl pivalate (Table 3, Entry 10). The title compound was prepared according to the general procedure from 6-amino-6-oxohexyl pivalate (1.0 mmol) and bromocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 50% EtOAc/hexanes). White solid. First run: 262 mg (88%). Second run: 263 mg (89%).

^1H NMR (500 MHz, $CDCl_3$) δ 5.34 (br s, 1H), 4.03 (td, J = 6.6, 0.8 Hz, 2H), 3.79 – 3.70 (m, 1H), 2.19 – 2.10 (m, 2H), 1.94 – 1.78 (m, 4H), 1.74 – 1.56 (m, 5H), 1.44 – 1.26 (m, 4H), 1.22 – 1.01 (m, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.6, 171.7, 64.2, 48.1, 38.7, 36.9, 33.3, 28.4, 27.2, 25.6, 25.52, 25.47, 24.9.

FT-IR (neat) 3291, 3075, 2930, 2898, 2854, 1728, 1638, 1541, 1480, 1451, 1398, 1363, 1284, 1151, 1039, 891 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{17}H_{31}NO_3$: 297.2, found: 297.3.



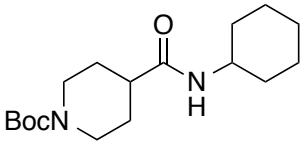
6-Oxo-6-(pentan-3-ylamino)hexyl pivalate (Table 3, Entry 11). The title compound was prepared according to the general procedure from 6-amino-6-oxohexyl pivalate (1.0 mmol) and 3-bromopentane (2.0 mmol). The product was purified by column chromatography (hexanes → 50% EtOAc/hexanes). White solid. First run: 177 mg (62%). Second run: 176 mg (62%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.13 (d, J = 9.1 Hz, 1H), 4.04 (t, J = 6.6 Hz, 2H), 3.83 – 3.74 (m, 1H), 2.22 – 2.14 (m, 2H), 1.76 – 1.59 (m, 4H), 1.60 – 1.48 (m, 2H), 1.44 – 1.28 (m, 4H), 1.18 (s, 9H), 0.88 (t, J = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.6, 172.4, 64.2, 51.8, 38.7, 36.9, 28.4, 27.5, 27.2, 25.7, 25.6, 10.2.

FT-IR (neat) 3291, 3077, 2962, 2934, 2874, 1728, 1635, 1544, 1480, 1459, 1284, 1152, 1038 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{16}H_{31}NO_3$: 285.2, found: 285.3.



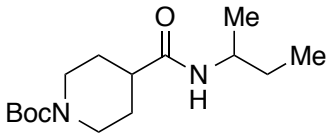
***t*-Butyl 4-(cyclohexylcarbamoyl)piperidine-1-carboxylate (Table 3, Entry 12).** The title compound was prepared according to the general procedure from *t*-butyl 4-carbamoylpiperidine-1-carboxylate (1.0 mmol) and bromocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 70% EtOAc/hexanes). Light-tan solid. First run: 283 mg (91%). Second run: 276 mg (89%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.36 (br s, 1H), 4.12 (br s, 2H), 3.79 – 3.70 (m, 1H), 2.72 (br s, 2H), 2.16 (tt, J = 11.6, 3.7 Hz, 1H), 1.92 – 1.84 (m, 2H), 1.81 – 1.74 (m, 3H), 1.74 – 1.53 (m, 4H), 1.48 – 1.42 (m, 9H), 1.42 – 1.29 (m, 2H), 1.21 – 1.03 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 154.7, 79.6, 48.0, 43.5, 33.2, 28.7, 28.4, 25.5, 24.8.

FT-IR (neat) 3249, 3082, 2929, 2853, 1693, 1634, 1558, 1441, 1415, 1389, 1363, 1338, 1217, 1162, 1122, 1091, 954, 944, 892, 870, 771, 719 cm^{-1}.

MS (ESI) *m*/*z* ($[M - C_4H_8 + H]^+$) calcd for $C_{13}H_{23}N_2O_3$: 255.2, found: 255.2.



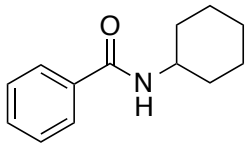
***t*-Butyl 4-(*s*-butylcarbamoyl)piperidine-1-carboxylate (Table 3, Entry 13).** The title compound was prepared according to the general procedure from *t*-butyl 4-carbamoylpiperidine-1-carboxylate (1.0 mmol) and 2-bromobutane (2.0 mmol). The product was purified by column chromatography (hexanes → 70% EtOAc/hexanes). Light-tan solid. First run: 243 mg (85%). Second run: 245 mg (85%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.27 (d, J = 8.7 Hz, 1H), 4.12 (br s, 2H), 3.90 (dq, J = 8.5, 6.6 Hz, 1H), 2.72 (br s, 2H), 2.23 – 2.13 (m, 1H), 1.83 – 1.75 (m, 2H), 1.67 – 1.56 (m, 2H), 1.44 (s, 11H), 1.10 (d, J = 6.6 Hz, 3H), 0.88 (t, J = 7.5 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 154.7, 79.6, 46.3, 43.6, 29.7, 28.8, 28.6, 28.4, 20.5, 10.3.

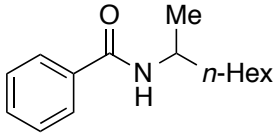
FT-IR (neat) 3281, 3072, 2972, 2928, 2877, 2858, 1683, 1634, 1544, 1432, 1365, 1282, 1216, 1177, 1126, 1078, 956, 942, 875, 761, 692 cm^{-1}.

MS (ESI) *m*/*z* ($[M - C_4H_8 + H]^+$) calcd for $C_{11}H_{21}N_2O_3$: 229.2, found: 229.1.



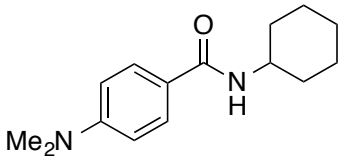
***N*-Cyclohexylbenzamide (Table 4, Entry 1) [1759-68-8].** The title compound was prepared according to the general procedure from benzamide (1.0 mmol) and iodocyclohexane (2.0 mmol). The product was purified by column chromatography (10% EtOAc/hexanes → 30% EtOAc/hexanes). Beige solid. First run: 178 mg (88%). Second run: 177 mg (87%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.73 (m, 2H), 7.51 – 7.46 (m, 1H), 7.45 – 7.40 (m, 2H), 5.95 (br s, 1H), 4.01 – 3.94 (m, 1H), 2.08 – 1.99 (m, 2H), 1.81 – 1.71 (m, 2H), 1.69 – 1.62 (m, 1H), 1.49 – 1.38 (m, 2H), 1.29 – 1.19 (m, 3H).



***N*-(Octan-2-yl)benzamide (Table 4, Entry 2) [103495-31-4].** The title compound was prepared according to the general procedure from benzamide (1.0 mmol) and 2-iodooctane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). Beige solid. First run: 143 mg (61%). Second run: 148 mg (63%).

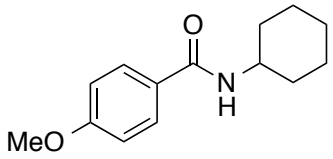
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.72 (m, 2H), 7.51 – 7.46 (m, 1H), 7.46 – 7.40 (m, 2H), 5.86 (d, J = 8.4 Hz, 1H), 4.24 – 4.14 (m, 1H), 1.58 – 1.48 (m, 2H), 1.41 – 1.25 (m, 8H), 1.23 (d, J = 6.6 Hz, 3H), 0.90 – 0.84 (m, 3H).



***N*-Cyclohexyl-4-(dimethylamino)benzamide (Table 4, Entry 3) [141557-50-8].** The title compound was prepared according to the general procedure from 4-(dimethylamino)benzamide (1.0 mmol) and iodocyclohexane (2.0 mmol). The product was

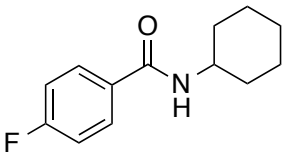
purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 209 mg (85%). Second run: 213 mg (86%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 – 7.60 (m, 2H), 6.69 – 6.61 (m, 2H), 5.83 (d, J = 8.1 Hz, 1H), 4.01 – 3.91 (m, 1H), 3.01 (s, 6H), 2.01 (dq, J = 12.1, 3.8 Hz, 2H), 1.79 – 1.59 (m, 3H), 1.48 – 1.36 (m, 2H), 1.27 – 1.14 (m, 3H).



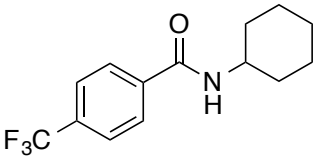
***N*-Cyclohexyl-4-methoxybenzamide (Table 4, Entry 4) [33739-91-2].** The title compound was prepared according to the general procedure from 4-methoxybenzamide (1.0 mmol) and iodocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 40% EtOAc/hexanes). White solid. First run: 184 mg (79%). Second run: 175 mg (75%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.67 (m, 2H), 6.96 – 6.86 (m, 2H), 5.91 (d, J = 8.1 Hz, 1H), 4.01 – 3.91 (m, 1H), 3.84 (s, 3H), 2.07 – 1.98 (m, 2H), 1.80 – 1.60 (m, 3H), 1.48 – 1.36 (m, 2H), 1.29 – 1.14 (m, 3H).



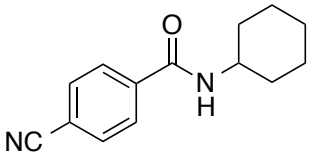
***N*-Cyclohexyl-4-fluorobenzamide (Table 4, Entry 5) [2342-50-9].** The title compound was prepared according to the general procedure from 4-fluorobenzamide (1.0 mmol) and iodocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 200 mg (91%). Second run: 200 mg (91%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.71 (m, 2H), 7.15 – 7.05 (m, 2H), 5.93 (d, J = 7.9 Hz, 1H), 4.01 – 3.91 (m, 1H), 2.07 – 1.98 (m, 2H), 1.81 – 1.61 (m, 3H), 1.48 – 1.36 (m, 2H), 1.29 – 1.14 (m, 3H).



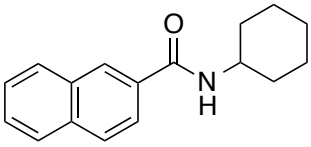
***N*-Cyclohexyl-4-(trifluoromethyl)benzamide (Table 4, Entry 6) [339094-67-6].** The title compound was prepared according to the general procedure from 4-(trifluoromethyl)benzamide (1.0 mmol) and iodocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 197 mg (73%). Second run: 211 mg (78%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.83 (m, 2H), 7.72 – 7.65 (m, 2H), 6.00 (d, J = 8.0 Hz, 1H), 4.03 – 4.93 (m, 1H), 2.09 – 2.00 (m, 2H), 1.82 – 1.72 (m, 2H), 1.72 – 1.62 (m, 1H), 1.50 – 1.37 (m, 2H), 1.32 – 1.11 (m, 3H).



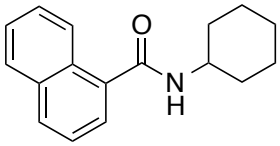
4-Cyano-*N*-cyclohexylbenzamide (Table 4, Entry 7) [167762-78-9]. The title compound was prepared according to the general procedure from 4-cyanobenzamide (1.0 mmol) and iodocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 40% EtOAc/hexanes). White solid. First run: 190 mg (83%). Second run: 179 mg (79%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 – 7.81 (m, 2H), 7.76 – 7.69 (m, 2H), 6.01 (d, J = 8.1 Hz, 1H), 4.02 – 3.92 (m, 1H), 2.08 – 1.99 (m, 2H), 1.82 – 1.62 (m, 3H), 1.49 – 1.36 (m, 2H), 1.30 – 1.14 (m, 3H).



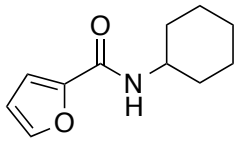
***N*-Cyclohexyl-2-naphthamide (Table 4, Entry 8) [82740-60-1].** The title compound was prepared according to the general procedure from 2-naphthamide (1.0 mmol) and iodocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 203 mg (80%). Second run: 197 mg (78%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 – 8.23 (m, 1H), 7.96 – 7.79 (m, 4H), 7.61 – 7.50 (m, 2H), 6.13 (d, J = 8.1 Hz, 1H), 4.10 – 4.00 (m, 1H), 2.13 – 2.04 (m, 2H), 1.84 – 1.64 (m, 3H), 1.52 – 1.40 (m, 2H), 1.35 – 1.17 (m, 3H).



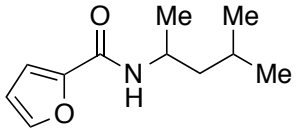
***N*-Cyclohexyl-1-naphthamide (Table 4, Entry 9) [32255-83-7].** The title compound was prepared according to the general procedure from 1-naphthamide (1.0 mmol) and iodocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 239 mg (94%). Second run: 237 mg (94%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 – 8.24 (m, 1H), 7.93 – 7.82 (m, 2H), 7.62 – 7.40 (m, 4H), 5.87 (d, J = 8.3 Hz, 1H), 4.15 – 4.06 (m, 1H), 2.17 – 2.08 (m, 2H), 1.83 – 1.63 (m, 3H), 1.54 – 1.41 (m, 2H), 1.33 – 1.15 (m, 3H).



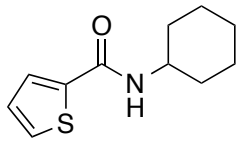
***N*-Cyclohexylfuran-2-carboxamide (Table 4, Entry 10) [10354-47-9].** The title compound was prepared according to the general procedure from furan-2-carboxamide (1.0 mmol) and iodocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 30% EtOAc/hexanes). Light-tan solid. First run: 165 mg (85%). Second run: 169 mg (88%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, J = 1.8, 0.8 Hz, 1H), 7.09 (dd, J = 3.5, 0.9 Hz, 1H), 6.49 (dd, J = 3.5, 1.8 Hz, 1H), 6.22 (br s, 1H), 3.99 – 3.89 (m, 1H), 2.07 – 1.95 (m, 2H), 1.80 – 1.60 (m, 3H), 1.48 – 1.35 (m, 2H), 1.30 – 1.14 (m, 3H).



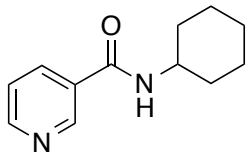
***N*-(4-methylpentan-2-yl)furan-2-carboxamide (Table 4, Entry 11) [100055-00-3].** The title compound was prepared according to the general procedure from furan-2-carboxamide (1.0 mmol) and 2-iodo-4-methylpentane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). Light-tan solid. First run: 135 mg (69%). Second run: 135 mg (69%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, J = 1.8, 0.8 Hz, 1H), 7.09 (dd, J = 3.4, 0.8 Hz, 1H), 6.49 (dd, J = 3.5, 1.8 Hz, 1H), 6.08 (br s, 1H), 4.31 – 4.18 (m, 1H), 1.73 – 1.62 (m, 1H), 1.50 – 1.42 (m, 1H), 1.37 – 1.28 (m, 1H), 1.22 (d, J = 6.6 Hz, 3H), 0.94 (t, J = 6.7 Hz, 6H).



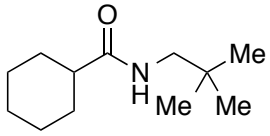
***N*-Cyclohexylthiophene-2-carboxamide (Table 4, Entry 12) [10354-42-4].** The title compound was prepared according to the general procedure from thiophene-2-carboxamide (1.0 mmol) and iodocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 30% EtOAc/hexanes). Light-tan solid. First run: 145 mg (69%). Second run: 154 mg (74%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 – 7.40 (m, 2H), 7.06 (dd, J = 5.0, 3.7 Hz, 1H), 5.83 (br s, 1H), 4.01 – 3.88 (m, 1H), 2.07 – 1.98 (m, 2H), 1.81 – 1.59 (m, 3H), 1.48 – 1.35 (m, 2H), 1.29 – 1.13 (m, 3H).



***N*-Cyclohexylnicotinamide (Table 4, Entry 13) [10354-56-0].** The title compound was prepared according to the general procedure from nicotinamide (1.0 mmol) and iodocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 100% EtOAc). White solid. First run: 167 mg (82%). Second run: 171 mg (84%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.94 (dd, J = 2.3, 0.9 Hz, 1H), 8.71 (dd, J = 4.8, 1.7 Hz, 1H), 8.12 – 8.08 (m, 1H), 7.37 (ddd, J = 7.9, 4.8, 0.9 Hz, 1H), 6.06 (d, J = 7.7 Hz, 1H), 4.04 –3.94 (m, 1H), 2.09 – 2.00 (m, 2H), 1.82 – 1.62 (m, 3H), 1.50 – 1.37 (m, 2H), 1.32 – 1.15 (m, 3H).



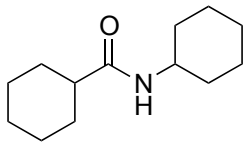
***N*-Neopentylcyclohexanecarboxamide (eq 3).** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and 1-bromo-2,2-dimethylpropane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). Off-white solid. First run: 154 mg (78%). Second run: 160 mg (81%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.45 (br s, 1H), 3.05 (d, J = 6.3 Hz, 2H), 2.09 (tt, J = 11.8, 3.5 Hz, 1H), 1.91 – 1.83 (m, 2H), 1.83 – 1.76 (m, 2H), 1.71 – 1.63 (m, 1H), 1.50 – 1.40 (m, 2H), 1.33 – 1.17 (m, 3H), 0.89 (s, 9H).

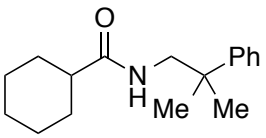
^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1, 110.0, 50.1, 45.9, 31.9, 29.9, 27.2, 25.8.

FT-IR (neat) 3280, 3090, 2852, 1644, 1558, 1208 cm^{-1}.

MS (ESI) *m*/*z* $(M + H)^+$ calcd for $C_{12}H_{24}NO$: 198.2, found: 198.2.



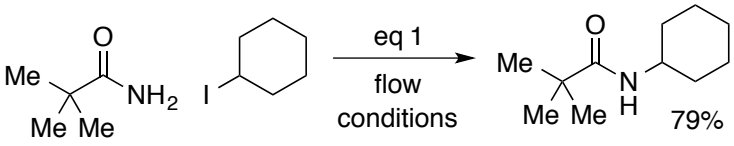
***N*-Cyclohexylcyclohexanecarboxamide (eq 3) [7474-36-4].** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and iodocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% AcOEt/hexanes). White solid. First run: 184 mg (88%). Second run: 182 mg (87%).

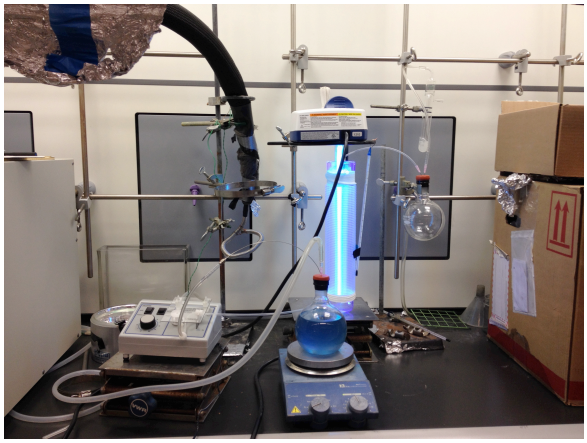


***N*-(2-Methyl-2-phenylpropyl)cyclohexanecarboxamide (eq 3) [1085543-93-6].** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and (1-chloro-2-methylpropan-2-yl)benzene (2.0 mmol) (reaction time: 48 h). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 172 mg (66%). Second run: 177 mg (68%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.31 (m, 4H), 7.30 – 7.19 (m, 1H), 5.09 (s, 1H), 3.46 (d, J = 6.0 Hz, 2H), 1.94 (tt, J = 11.8, 3.3 Hz, 1H), 1.85 – 1.58 (m, 5H), 1.33 (s, 6H), 1.39 – 1.13 (m, 5H).

Flow reaction (eq 4)

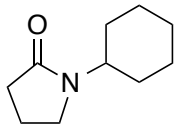




A continuous-flow reactor was constructed based on the design of Booker-Milburn.[6] Fluorinated ethylene propylene (FEP) tubing (4 mm o.d., 3 mm i.d., 15 m length; from Idex Health & Science, catalog #1679L) was wrapped around a homemade quartz immersion well (65 mm o.d., 45 mm i.d., 30 cm length), leaving 30 cm of tubing free at each end. The internal volume of the reactor was ~100 mL. The ends of the tubing were secured to the well with Teflon tape. The top end of the tubing was fitted with a needle and then connected to a receiver (500-mL nitrogen-filled round-bottom flask). The bottom end of the tubing was connected to a Peristaltic Metering Pump (Grainger, item #3KYX2), and the pump was connected to the container of starting-material solution through a long needle. The reaction temperature was kept at ~r.t. by applying an air flow through the well (from bottom to top). A 36-watt UVC lamp (UV100A 1059 from Honeywell) was placed inside the immersion well as shown in the picture.

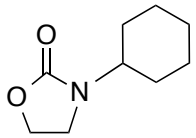
(6) (a) Hook, B. D. A.; Dohle, W.; Hirst, P. R.; Pickworth, M.; Berry, M. B.; Booker-Milburn, K. I. *J. Org. Chem.* **2005,** *70,* 7558–7564. (b) Willumstad, T. P.; Haze, O.; Mak, X. Y.; Lam, T. Y.; Wang, Y.-P.; Danheiser, R. L. *J. Org. Chem.* **2013**, *78*, 11450–11469.

A 500-mL flat-bottom flask was charged with CuI (1.37 g, 7.00 mmol, 0.10 equiv), pivalamide (7.07 g, 70.0 mmol), and LiO*t*-Bu (11.2 g, 140 mmol, 2.0 equiv). The flask was capped with a rubber septum, the joint was wrapped with electrical tape, and the flask was evacuated and backfilled with nitrogen (3 cycles). Next, CH_3CN (380 mL), DMF (54.0 mL), and iodocyclohexane (29.4 g, 140 mmol, 2.0 equiv) were added in turn by syringe. The flask was detached from the nitrogen line, and the puncture holes of the septum were covered with vacuum grease. The resulting mixture was stirred vigorously for 5 min, and then connected to the pump. The entire system was flushed with nitrogen for 10 min. The stirring starting material was pumped into the photoreactor at a rate of 0.3 mL/min. Upon completion, the collected reaction mixture was filtered through a short pad of silica and concentrated under reduced pressure. The residue was purified by column chromatography (hexanes → 20% EtOAc/hexanes), which afforded 10.1 g of a white solid (79% yield).



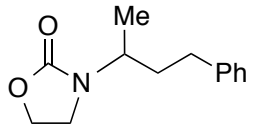
1-Cyclohexylpyrrolidin-2-one (eq 5) [6837-24-7]. The title compound was prepared according to the general procedure (except that no DMF was used; only CH_3CN (6.2 mL)) from 2-pyrrolidone (1.0 mmol) and bromocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 70% EtOAc/hexanes). Light-brown oil. First run: 149 mg (89%). Second run: 147 mg (88%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.99 – 3.86 (m, 1H), 3.36 – 3.28 (m, 2H), 2.41 – 2.34 (m, 2H), 2.02 – 1.92 (m, 2H), 1.84 – 1.61 (m, 5H), 1.45 – 1.28 (m, 4H), 1.16 – 1.00 (m, 1H).



3-Cyclohexyloxazolidin-2-one (eq 6) [55390-61-9]. The title compound was prepared according to the general procedure (except that no DMF was used; only CH_3CN (6.2 mL)) from oxazolidin-2-one (1.0 mmol) and bromocyclohexane. The product was purified by column chromatography (hexanes → 70% EtOAc/hexanes). Light-brown oil. First run: 153 mg (91%). Second run: 150 mg (89%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.36 – 4.25 (m, 2H), 3.72 – 3.63 (m, 1H), 3.57 – 3.46 (m, 2H), 1.87 – 1.74 (m, 4H), 1.72 – 1.62 (m, 1H), 1.45 – 1.28 (m, 4H), 1.17 – 1.01 (m, 1H).



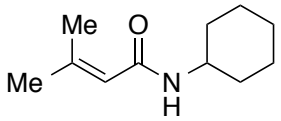
3-(4-Phenylbutan-2-yl)oxazolidin-2-one (eq 6). The title compound was prepared according to the general procedure from oxazolidin-2-one (1.0 mmol) and (3-bromobutyl)benzene (2.0 mmol). The product was purified by column chromatography (hexanes → 70% EtOAc/hexanes). Light-tan oil. First run: 196 mg (89%). Second run: 185 mg (85%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.16 (m, 5H), 4.32 – 4.26 (m, 1H), 4.21 – 4.14 (m, 1H), 4.06 – 3.98 (m, 1H), 3.48 (ddd, J = 9.3, 8.2, 7.5 Hz, 1H), 3.35 (ddd, J = 9.2, 8.2, 6.0 Hz, 1H), 2.73 – 2.55 (m, 2H), 1.92 – 1.72 (m, 2H), 1.20 (d, J = 6.8 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.0, 141.4, 128.5, 128.3, 126.0, 61.9, 49.0, 39.6, 35.7, 32.9, 18.1.

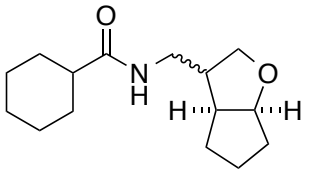
FT-IR (neat) 3025, 2969, 2925, 1737, 1494, 1482, 1453, 1422, 1386, 1252, 1052, 1029, 761, 699 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{13}H_{17}NO_2$: 219.1, found: 219.2.



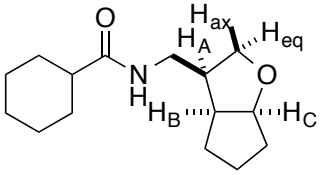
***N*-Cyclohexyl-3-methylbut-2-enamide (eq 7) [15745-12-7].** The title compound was prepared according to the general procedure from 3-methylbut-2-enamide (1.0 mmol) and bromocyclohexane (2.0 mmol). The product was purified by column chromatography (hexanes → 20% EtOAc/hexanes). White solid. First run: 155 mg (85%). Second run: 151 mg (83%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.53 – 5.50 (m, 1H), 5.23 (br s, 1H), 3.84 – 3.75 (m, 1H), 2.13 (d, J = 1.3 Hz, 3H), 1.97 – 1.86 (m, 2H), 1.82 (d, J = 1.3 Hz, 3H), 1.77 – 1.56 (m, 3H), 1.42 – 1.31 (m, 2H), 1.23 – 1.05 (m, 3H).



***N*-((Hexahydro-2*H*-cyclopenta[b]furan-3-yl)methyl)cyclohexanecarboxamide (eq 10).** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and *trans*-1-(allyloxy)-2-bromocyclopentane (2.0 mmol). The ratio of diastereomers was determined by GC analysis of the unpurified reaction mixture. The product was isolated as a mixture of diastereomers by column chromatography (30% EtOAc/hexanes → 75% EtOAc/hexanes). Yellow solid. First run: 214 mg (85%, 71:29). Second run: 219 mg (87%, 72:28).

Major diastereomer. The major diastereomer could be purified by preparative HPLC (IA column, 5% IPA/hexanes).



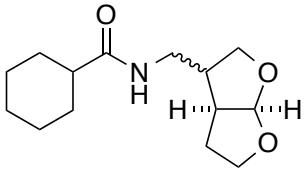
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.55 (br s, 1H), 4.50 (td, J = 5.8, 2.2 Hz, 1H), 3.84 (dd, J = 8.4, 7.1 Hz, 1H), 3.45 (t, J = 8.8 Hz, 1H), 3.38 – 3.25 (m, 2H), 2.59 – 2.46 (m, 2H), 2.05 (tt, J = 11.8, 3.5 Hz, 1H), 1.88 – 1.13 (m, 16H).

2D NOESY (500 MHz, $CDCl_3$) δ [2.51 (H_A), 3.84 (H_{eq})], [2.51 (H_A), 4.51 (H_C)], [2.56 (H_B), 4.51 (H_C)], [3.85 (H_{eq}), 2.51 (H_A)], [3.84 (H_{eq}), 4.51 (H_C)], [4.51 (H_C), 2.56 (H_B)], [4.51 (H_C), 3.85 (H_{eq})].

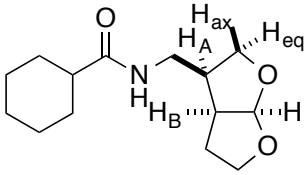
^{13}C NMR (75 MHz,$CDCl_3$) δ 176.1, 86.3, 70.7, 45.54, 45.48, 43.1, 38.3, 34.2, 29.7, 26.1, 25.7, 25.4.

FT-IR (neat) 3280, 3089, 2853, 1638, 1549, 1462, 1448, 1435, 1258, 1217, 1040 cm^{-1}.

MS (ESI) *m*/*z* $(M + H)^+$ calcd for $C_{15}H_{26}NO_2$: 252.2, found: 252.2.



***N*-((Hexahydrofuro[2,3-*b*]furan-3-yl)methyl)cyclohexanecarboxamide (eq 10).** The title compound was prepared according to the general procedure from cyclohexanecarboxamide (1.0 mmol) and *trans*-2-(allyloxy)-3-bromotetrahydrofuran (2.0 mmol). The ratio of diastereomers was determined by ^{1}H NMR analysis of the unpurified reaction mixture. The product was isolated by column chromatography (75% EtOAc/hexanes → EtOAc). Yellow solid. First run: 234 mg (92%, 96:4). Second run: 217 mg (86%, 96:4).

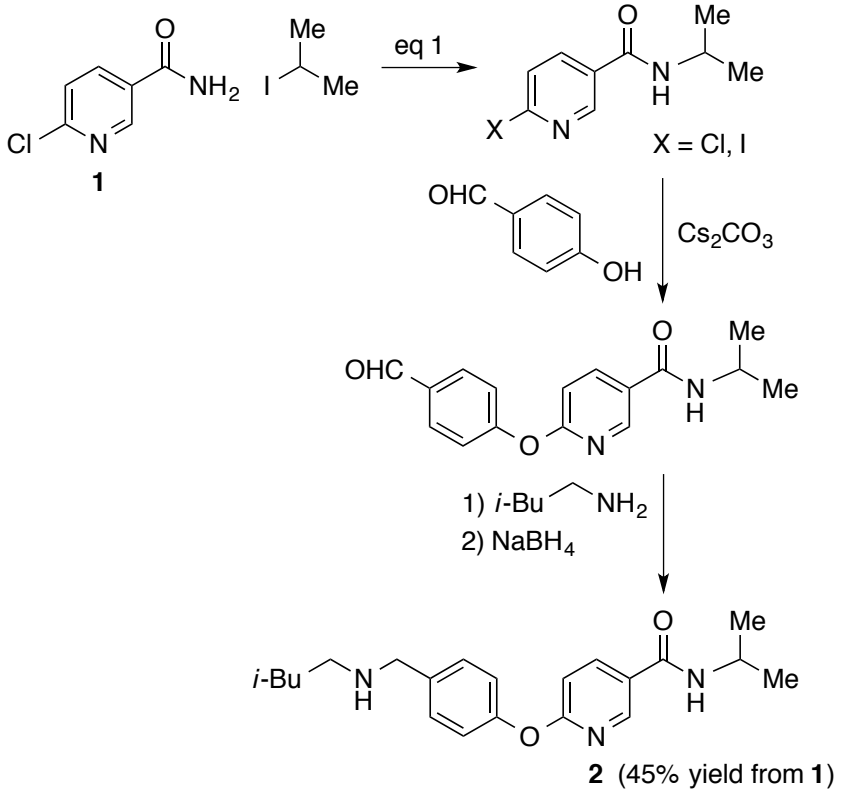


^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (d, J = 5.0 Hz, 1H), 5.49 (s, 1H), 3.95 (dd, J = 8.7, 7.3 Hz, 1H), 3.92 – 3.86 (m, 2H), 3.55 (dd, J = 11.2, 8.6 Hz, 1H), 3.47 – 3.39 (m, 1H), 3.36 – 3.29 (m, 1H), 2.87 – 2.80 (m, 1H), 2.58 – 2.48 (m, 1H), 2.06 (tt, J = 11.8, 3.4 Hz, 1H), 1.97 – 1.59 (m, 7H), 1.47 – 1.37 (m, 2H), 1.30 – 1.19 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 109.8, 70.9, 69.2, 45.5, 44.5, 42.5, 37.7, 29.72, 29.68, 25.7, 25.1.

FT-IR (neat) 3323, 2977, 2883, 2852, 1644, 1541, 1448, 1442, 1021, 1004, 955 cm^{-1}.

MS (ESI) *m*/*z* $(M + H)^+$ calcd for $C_{14}H_{24}NO_3$: 254.2, found: 254.2.



Synthesis of an opioid receptor antagonist (2; Figure 1) [676501-63-6].

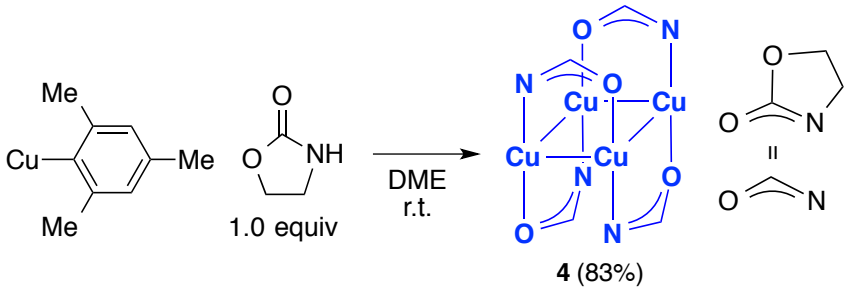
Step 1: The N-alkylation was performed according to the general procedure in four batches with 6-chloronicotinamide (1.0 mmol) and 2-iodopropane (2.0 mmol) (reaction time: 9 h). The combined product was isolated by column chromatography (hexanes → 50% EtOAc/hexanes), which afforded 520 mg of a mixture of 6-chloro-*N*-isopropylnicotinamide and 6-iodo-*N*-isopropylnicotinamide (2.5:1), which was subjected to the next step without separation.

Step 2: In a nitrogen-filled glovebox, a 20-mL vial was charged with the 6-halo-*N*-isopropylnicotinamides (520 mg), 4-hydroxybenzaldehyde (478 mg, 3.92 mmol), Cs_2CO_3 (1.70 g, 5.20 mmol), and DMF (5.0 mL). The vial was tightly sealed with a PTFE-lined septum cap, taken out of the glovebox, and heated at 125 °C for 12 h. Next, the reaction mixture was purified by column chromatography (hexanes → 60% EtOAc/hexanes), which furnished 541 mg of 6-(4-formylphenoxy)-*N*-isopropylnicotinamide as a white solid (47% over 2 steps).

Step 3 and 4: A mixture of 6-(4-formylphenoxy)-*N*-isopropylnicotinamide (541 mg, 1.90 mmol), isopentylamine (248 mg, 2.85 mmol, 1.50 equiv), and Na_2SO_4 (2.00 g, 14.1 mmol, 7.41 equiv) in CH_2Cl_2 (5.0 mL) was stirred at room temperature for 4 h. The solid was removed by filtration and rinsed with CH_2Cl_2 (2x10 mL). The combined organic layers were concentrated under reduced pressure, and then the residue was dissolved in MeOH (5.0 mL). $NaBH_4$ (76.0 mg, 2.00 mmol) was added portionwise to maintain the reaction temperature around ambient temperature. The mixture was stirred for 2 h, and then it was concentrated. The residue was dissolved in CH_2Cl_2 (150 mL), and the resulting solution was washed with water (2x30 mL), dried over $MgSO_4$, and concentrated to afford pure **2** (640 mg, 95% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (dd, J = 2.6, 0.7 Hz, 1H), 8.10 (dd, J = 8.6, 2.5 Hz, 1H), 7.41 – 7.33 (m, 2H), 7.13 – 7.05 (m, 2H), 6.92 (dd, J = 8.6, 0.7 Hz, 1H), 5.79 (d, J = 7.8 Hz, 1H), 4.33 – 4.23 (m, 1H), 3.81 (s, 2H), 2.72 – 2.62 (m, 2H), 1.70 – 1.60 (m, 1H), 1.46 – 1.36 (m, 2H), 1.27 (d, J = 6.6 Hz, 6H), 0.91 (d, J = 6.6 Hz, 6H).

IV. Synthesis and Crystal Structure of Complex 4



Complex 4. In a nitrogen-filled glovebox, a 20-mL vial was charged with mesitylcopper(I) (183 mg, 1.00 mmol) and 2-oxazolidone (87.0 mg, 1.00 mmol, 1.00 equiv). 1,2-Dimethoxyethane (18.0 mL) was added, and the reaction mixture was stirred at room temperature for 4 h, resulting in a pale-yellow precipitate. The suspension was allowed to settle overnight, and then the solvent was decanted. The solid was washed with pentane (2x3 mL) and dried under vacuum, affording complex **4** as a pale-yellow solid (124 mg, 83% yield).

^{1}H NMR (500 MHz, DMF-d$_7$) δ 4.64 (br s, 8H), 3.82 (br s, 8H).

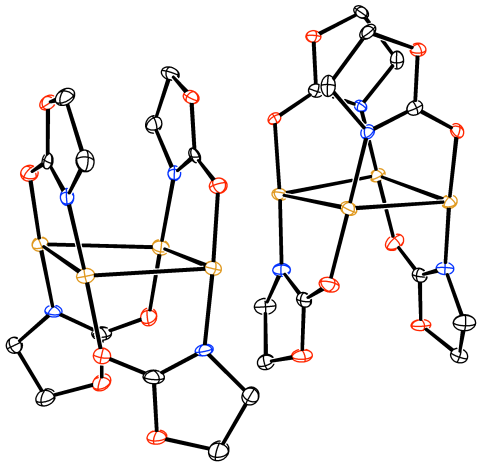
Anal. calcd for $C_{12}H_{16}Cu_4N_4O_8$: C, 24.08; H, 2.69; N, 9.36. Found: C, 24.23; H, 2.69; N, 9.33.

Preparation of X-ray quality crystals. In a nitrogen-filled glovebox, a 4-mL vial was charged with mesitylcopper(I) (37 mg, 0.20 mmol, 1.0 equiv) and 2-oxazolidone (17 mg, 0.20 mmol, 1.0 equiv). 1,2-Dimethoxyethane (4.0 mL) was added, and the reaction mixture was stirred at room temperature for 30 min. The resulting suspension was filtered through an acrodisc, and the filtrate was kept at room temperature for 24 h, furnishing pale-yellow crystals that were suitable for X-ray diffraction.

A crystal of $C_{12}H_{16}Cu_4N_4O_8$ was selected and mounted in a nylon loop in immersion oil. All measurements were made on a Bruker APEX-II with filtered Mo-Kα radiation at a temperature of 100 K. Using Olex2,[7] the structure was solved with the ShelXS[8] structure solution program using Direct Methods and refined with the ShelXL[8] refinement package using Least Squares minimization.

(7) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Cryst.* **2009**, *42*, 339–341.

(8) Sheldrick, G. M. *Acta Cryst. A* **2008**, *64*, 112–122.



Expanded view of the two independent tetramers.

Table 1. Crystal data and structure refinement for crystal_001.

Identification code	crystal_001	
Empirical formula	$C_{12}H_{16}Cu_4N_4O_8$	
Formula weight	598.45	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Tetragonal	
Space group	I -4 2 d	
Unit cell dimensions	a = 12.2871(2) Å	α = 90°
	b = 12.2871(2) Å	β = 90°
	c = 46.5540(12) Å	γ = 90°
Volume	7028.4(3) $Å^3$	
Z	16	
Density (calculated)	2.262 Mg/m^3	
Absorption coefficient	4.828 mm^{-1}	
F(000)	4736	
Crystal size	0.11 x 0.1 x 0.01 mm^3	
Theta range for data collection	1.714 to 27.863°.	
Index ranges	-15<=h<=16, -16<=k<=16, -61<=l<=61	
Reflections collected	33381	
Independent reflections	4205 [R(int) = 0.0760]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.7918	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4205 / 0 / 253	
Goodness-of-fit on F^2	1.026	
Final R indices [I>2sigma(I)]	R1 = 0.0332, wR2 = 0.0636	
R indices (all data)	R1 = 0.0464, wR2 = 0.0677	
Absolute structure parameter	-0.004(11)	
Largest diff. peak and hole	0.644 and -0.437 $e/Å^{-3}$	

Table 2. Atomic coordinates (x10^4) and equivalent isotropic displacement parameters (Å^{2}x10^3) for crystal_001. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cu(3)	5996(1)	3621(1)	3891(1)	13(1)
Cu(2)	3443(1)	1199(1)	4065(1)	16(1)
Cu(4)	6274(1)	5921(1)	3855(1)	14(1)
Cu(1)	5743(1)	991(1)	4092(1)	19(1)
O(5)	6368(3)	3674(3)	3501(1)	14(1)
O(3)	3714(3)	1432(3)	3674(1)	17(1)
O(8)	4527(3)	3451(3)	4666(1)	18(1)
O(4)	4720(3)	1302(3)	3276(1)	16(1)
O(6)	6297(3)	4498(3)	3076(1)	13(1)
O(7)	3740(3)	3680(3)	4240(1)	19(1)
O(1)	6053(4)	819(3)	4481(1)	26(1)
N(2)	6829(4)	-902(4)	4450(1)	15(1)
O(2)	6755(4)	26(4)	4868(1)	31(1)
N(4)	6327(4)	5555(4)	3469(1)	11(1)
N(1)	5591(4)	1250(4)	3702(1)	13(1)
N(3)	5615(4)	3490(4)	4276(1)	14(1)
C(10)	6336(4)	4572(4)	3367(1)	11(1)
C(7)	4626(5)	3544(4)	4375(1)	13(1)
C(4)	4666(5)	1333(4)	3567(1)	14(1)
C(5)	5884(5)	1312(5)	3201(1)	20(1)
C(12)	6212(5)	6318(4)	3228(1)	15(1)
C(11)	6402(5)	5598(4)	2966(1)	16(1)
C(1)	6530(6)	-14(5)	4580(1)	21(1)
C(9)	6350(5)	3432(5)	4524(1)	19(1)
C(6)	6465(5)	1154(5)	3485(1)	19(1)
C(3)	7430(5)	-1567(5)	4660(1)	18(1)
C(8)	5591(5)	3125(5)	4770(1)	18(1)
C(2)	7143(6)	-1040(6)	4946(1)	34(2)

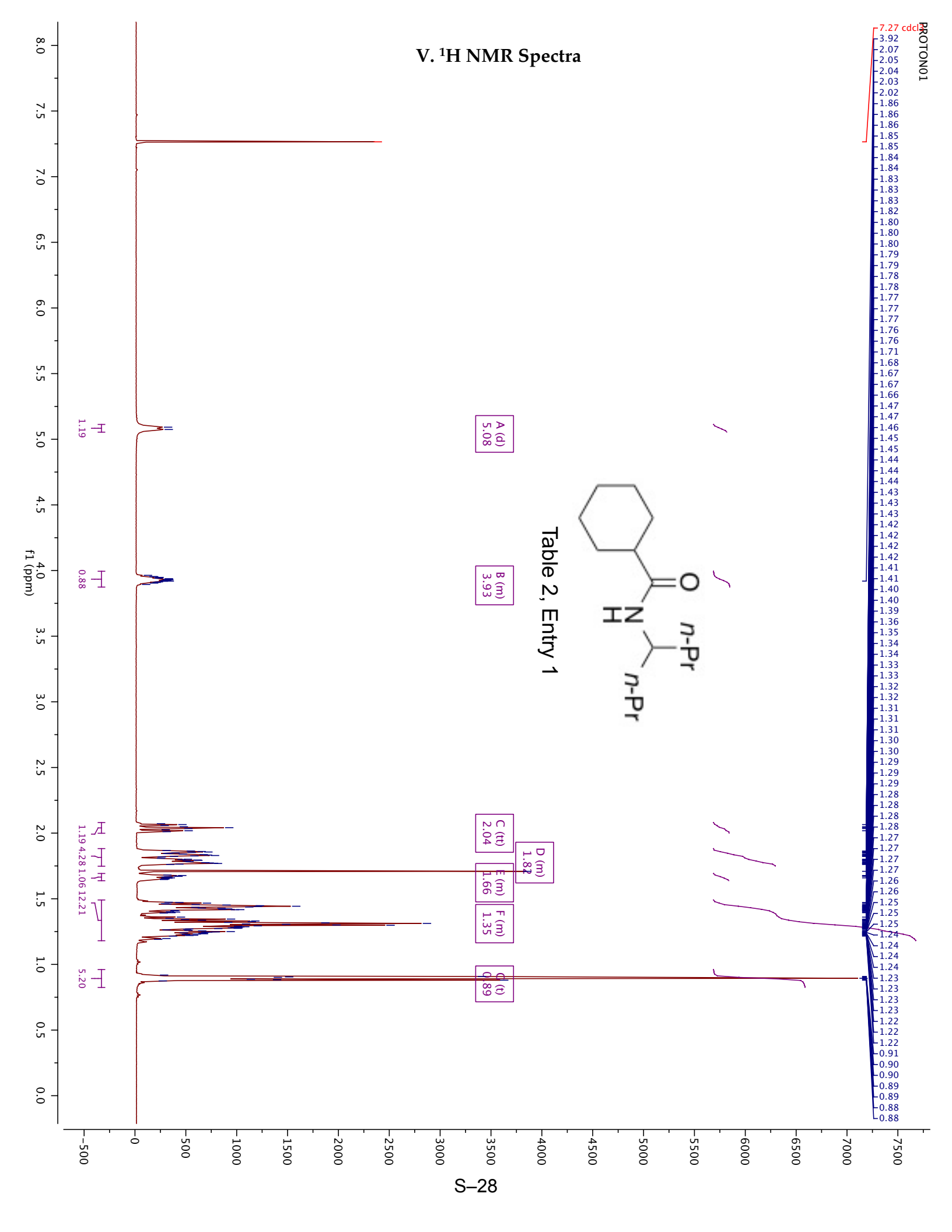
Table 3. Anisotropic displacement parameters ($Å^2x10^3$) for crystal_001. The anisotropic displacement factor exponent takes the form: $-2ð^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

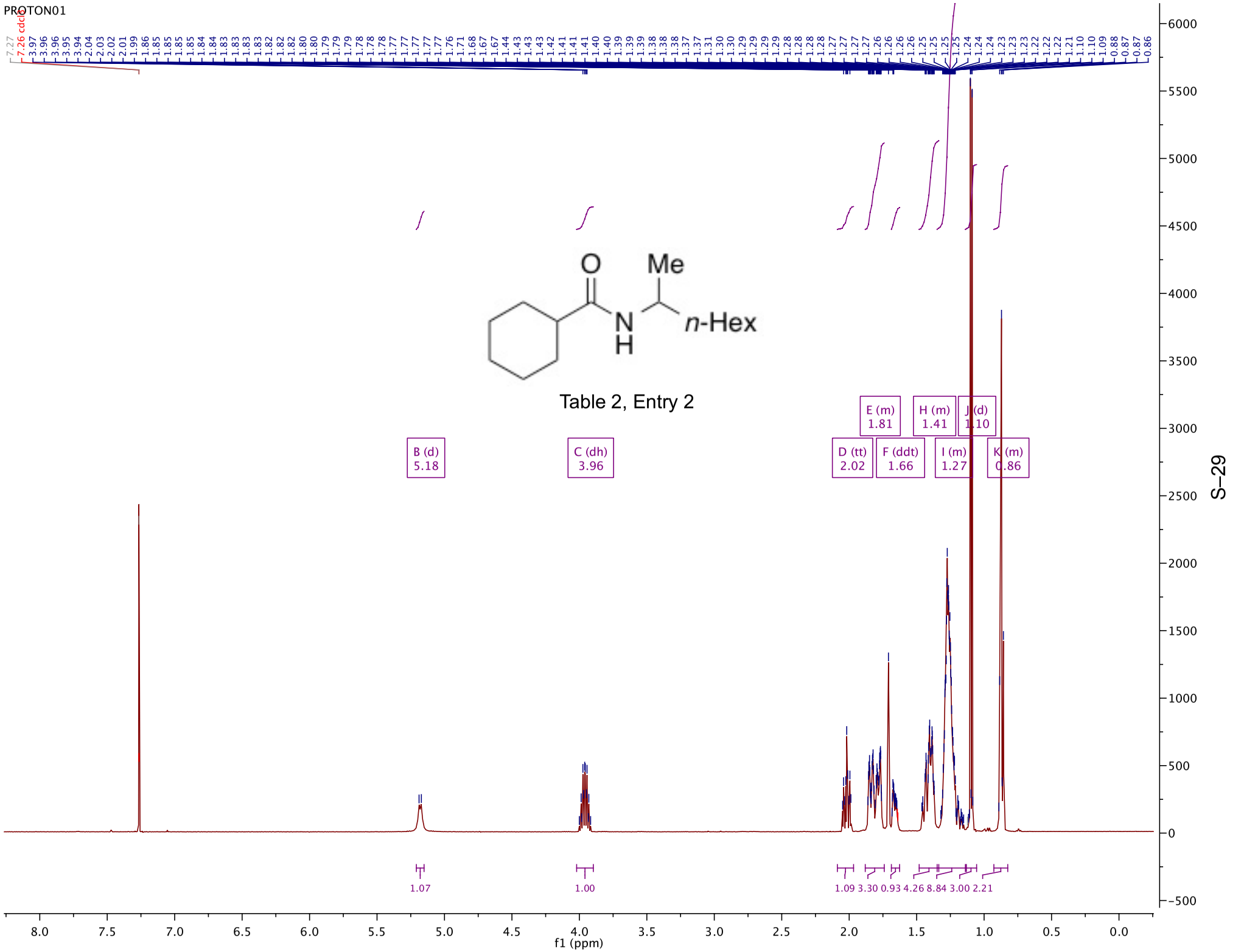
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cu(3)	14(1)	15(1)	10(1)	2(1)	2(1)	0(1)
Cu(2)	23(1)	15(1)	11(1)	2(1)	2(1)	1(1)
Cu(4)	16(1)	16(1)	11(1)	-3(1)	0(1)	1(1)
Cu(1)	25(1)	18(1)	12(1)	0(1)	-3(1)	3(1)
O(5)	17(2)	13(2)	10(2)	1(2)	6(2)	4(2)
O(3)	17(2)	19(2)	14(2)	1(2)	2(2)	3(2)
O(8)	18(2)	28(2)	8(2)	-1(2)	-1(2)	0(2)
O(4)	20(2)	18(2)	10(2)	4(2)	2(2)	7(2)
O(6)	17(2)	14(2)	9(2)	1(1)	2(2)	0(2)
O(7)	15(2)	27(2)	15(2)	7(2)	3(2)	3(2)
O(1)	45(3)	20(2)	14(2)	-3(2)	-6(2)	11(2)
N(2)	18(3)	19(3)	7(2)	1(2)	-2(2)	2(2)
O(2)	53(3)	31(3)	9(2)	-4(2)	-6(2)	20(2)
N(4)	13(2)	11(2)	10(2)	3(2)	2(2)	1(2)
N(1)	15(2)	10(2)	14(2)	1(2)	3(2)	2(2)
N(3)	14(2)	18(3)	10(2)	-1(2)	-1(2)	-3(2)
C(10)	4(3)	17(3)	12(3)	2(2)	1(2)	0(2)
C(7)	19(3)	8(3)	13(3)	0(2)	0(2)	-5(2)
C(4)	24(3)	4(3)	13(3)	3(2)	1(2)	-2(2)
C(5)	25(3)	22(3)	12(3)	6(2)	5(2)	6(3)
C(12)	11(3)	11(3)	23(3)	3(2)	5(2)	0(2)
C(11)	17(3)	18(3)	11(3)	6(2)	1(2)	5(3)
C(1)	29(4)	23(3)	9(3)	-1(2)	-1(3)	-1(3)
C(9)	13(3)	29(4)	17(3)	-1(2)	-1(2)	-6(3)
C(6)	18(3)	17(3)	21(3)	1(2)	7(2)	2(3)
C(3)	20(3)	18(3)	16(3)	1(2)	0(2)	4(2)
C(8)	21(3)	19(3)	14(3)	-2(2)	0(2)	1(3)
C(2)	54(5)	34(4)	14(3)	0(3)	1(3)	21(4)

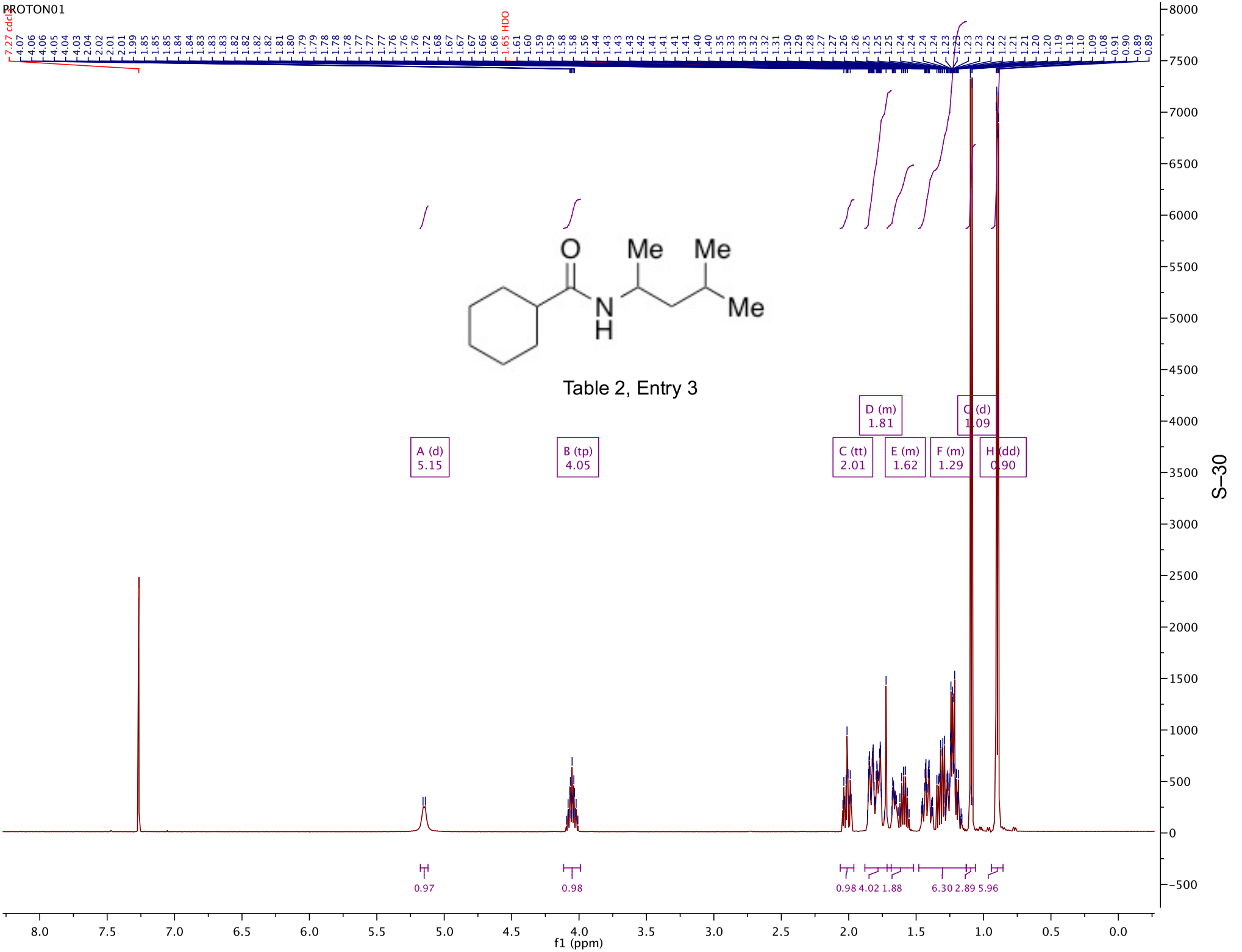
Table 4. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x10^3) for crystal_001.

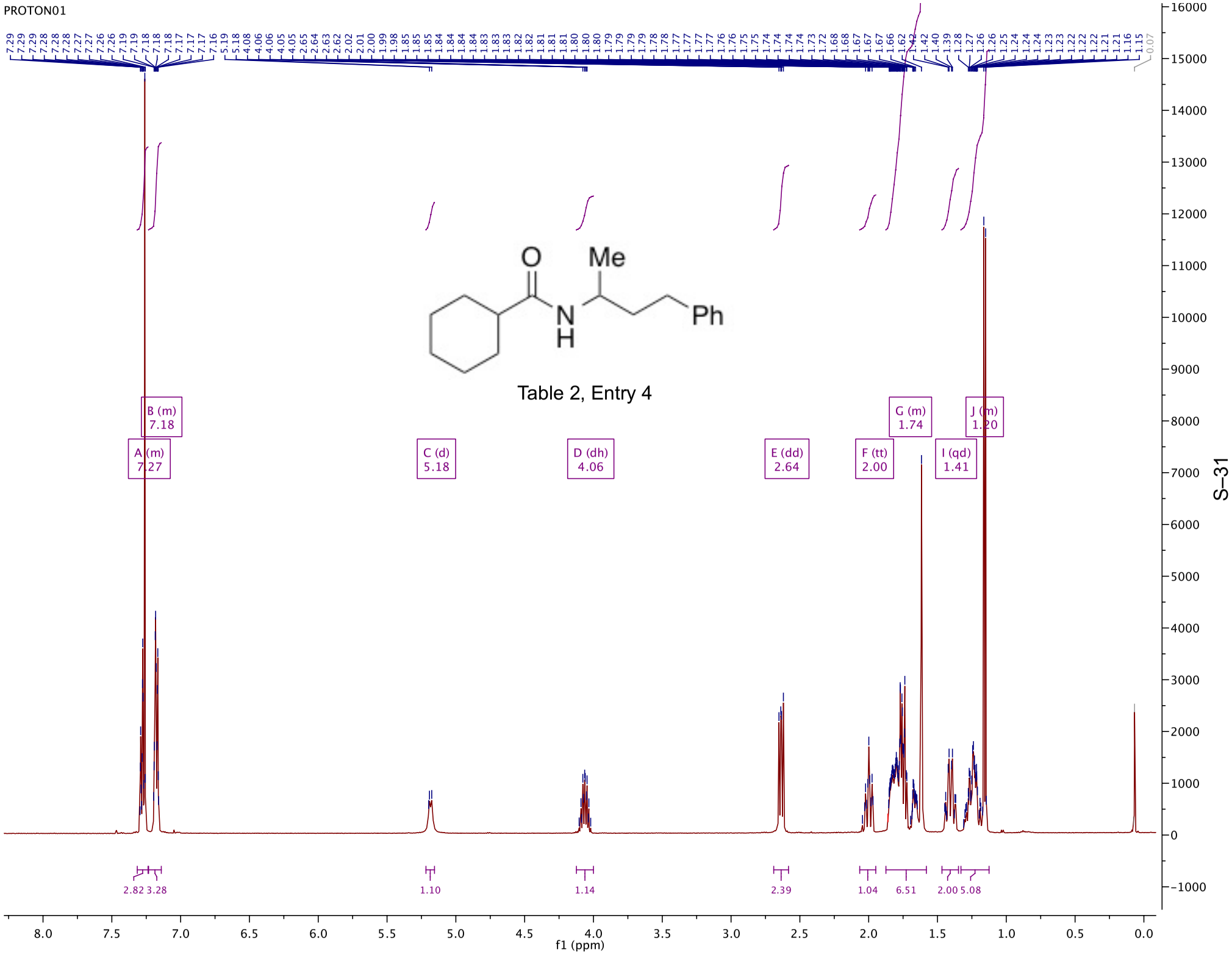
	x	y	z	U(eq)
H(5A)	6091	2014	3113	23
H(5B)	6060	716	3066	23
H(12A)	6761	6906	3239	18
H(12B)	5476	6645	3224	18
H(11A)	5852	5744	2815	19
H(11B)	7137	5720	2884	19
H(9A)	6705	4143	4560	23
H(9B)	6918	2871	4496	23
H(6A)	6813	428	3494	23
H(6B)	7027	1720	3514	23
H(3A)	8223	-1536	4624	21
H(3B)	7189	-2335	4654	21
H(8A)	5616	2333	4809	22
H(8B)	5783	3523	4948	22
H(2A)	6571	-1459	5046	41
H(2B)	7791	-989	5071	41

V. ^{1}H NMR Spectra




PROTON01
O
Me
N
H
n-Hex
Table 2, Entry 2
B (d) 5.18
C (dh) 3.96
E (m) 1.81
H (m) 1.41
J (d) 1.10
D (tt) 2.02
F (ddt) 1.66
I (m) 1.27
K (m) 0.86
1.07
1.00
1.09 3.30 0.93 4.26 8.84 3.00 2.21
f1 (ppm)


PROTON01
O
Me
Me
N
H
Me
Table 2, Entry 3
A (d)
5.15
B (tp)
4.05
C (tt)
2.01
D (m)
1.81
E (m)
1.62
F (m)
1.29
G (d)
1.09
H (dd)
0.90
0.97
0.98
0.98 4.02 1.88
6.30 2.89 5.96
f1 (ppm)
S–30


PROTON01
O
Me
N
H
Ph
Table 2, Entry 4
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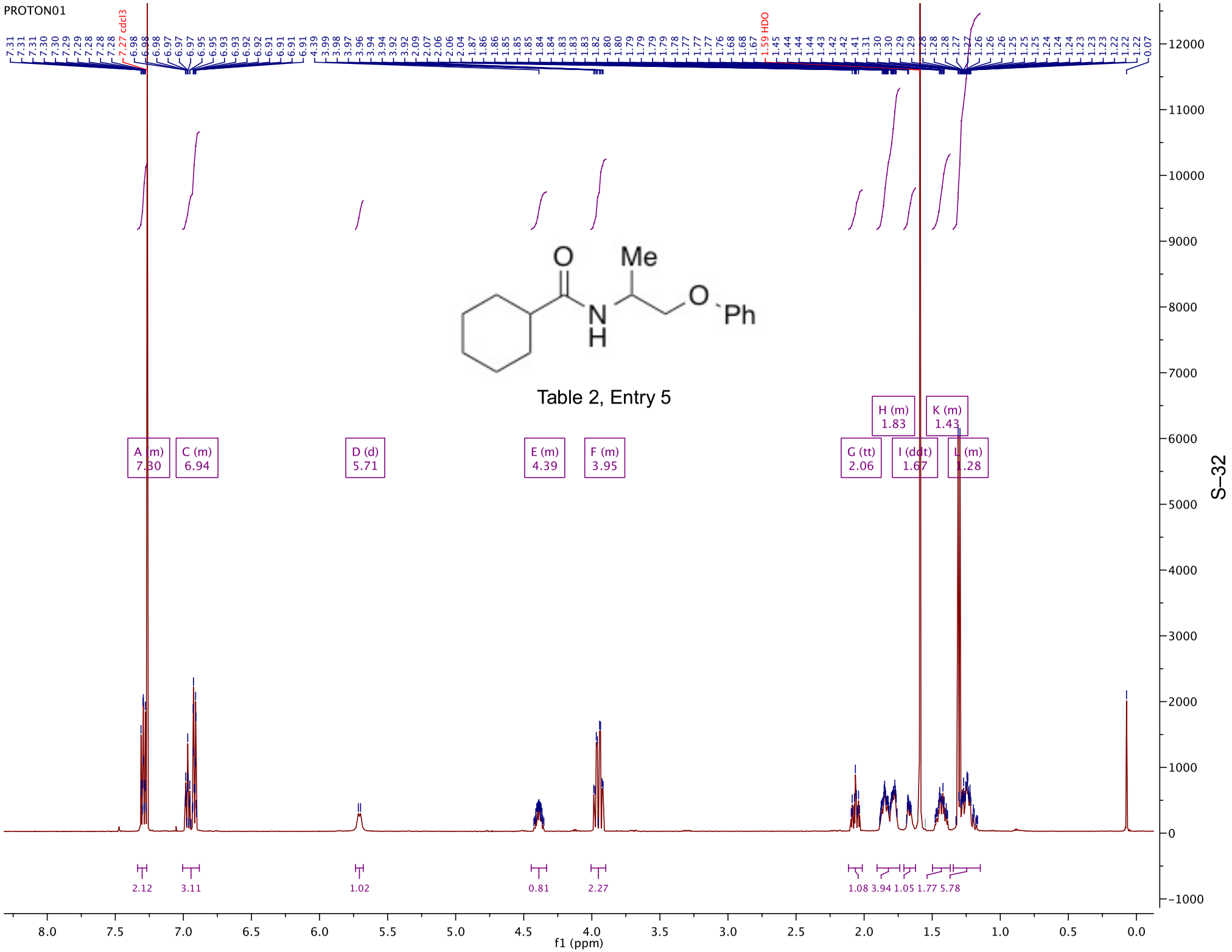
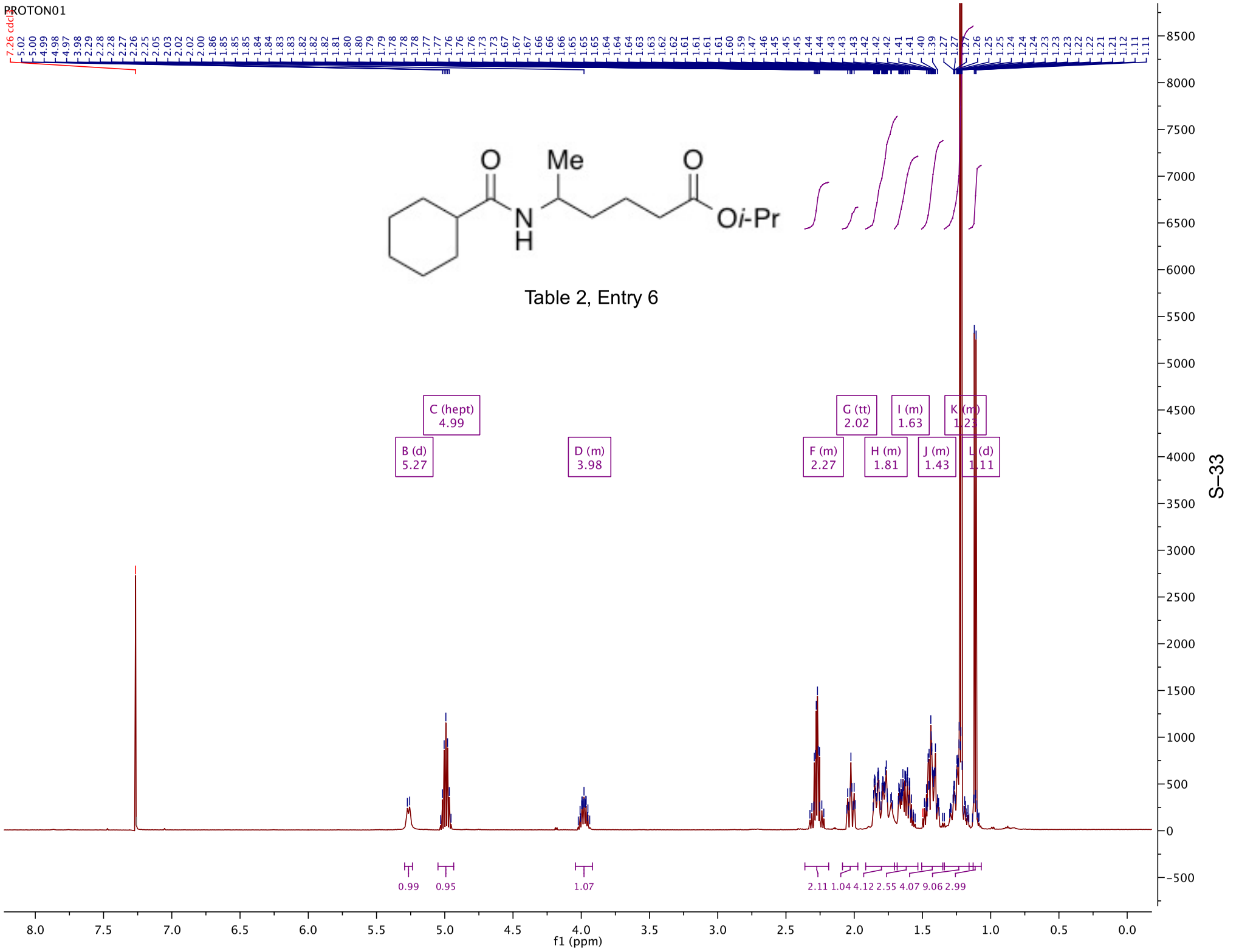
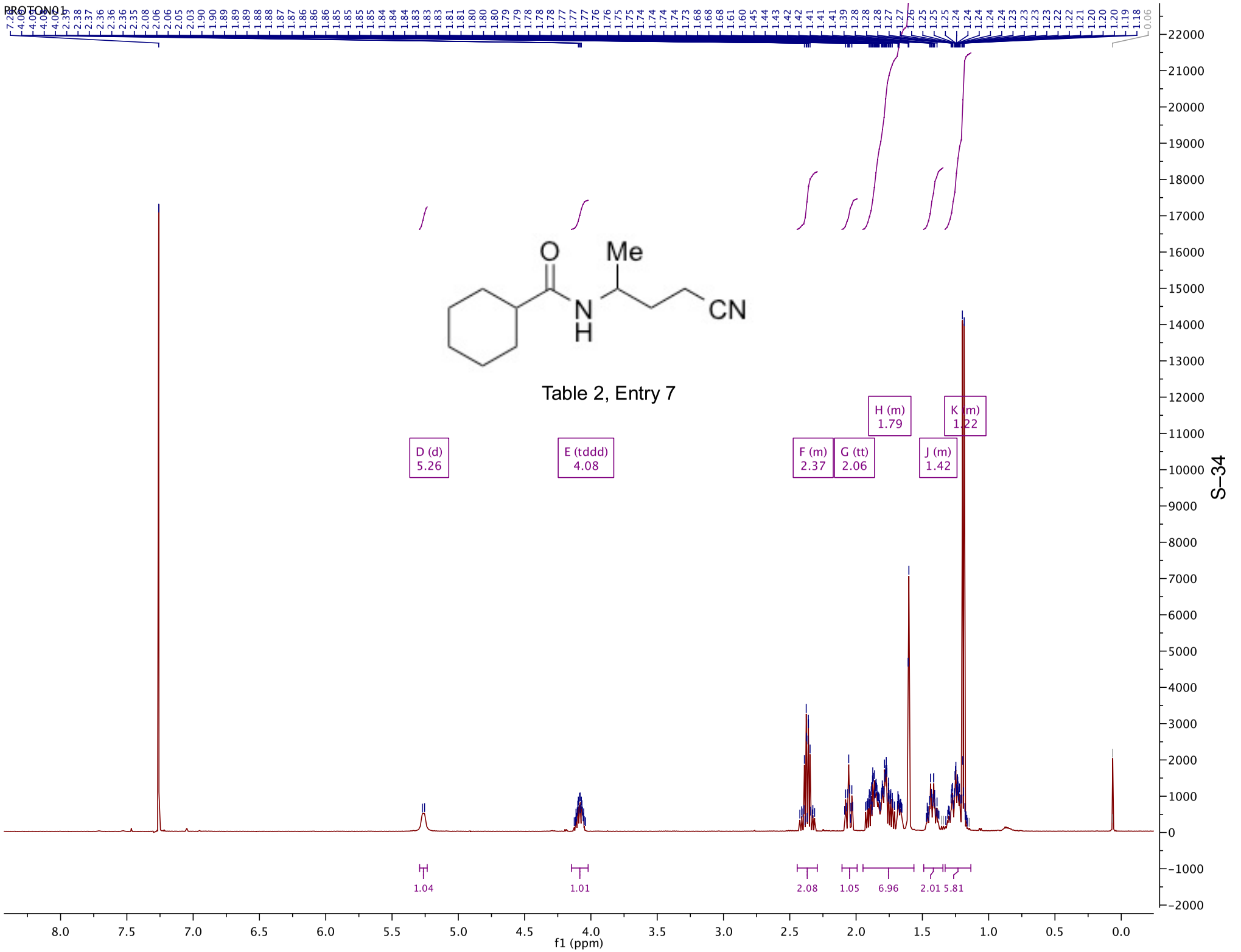
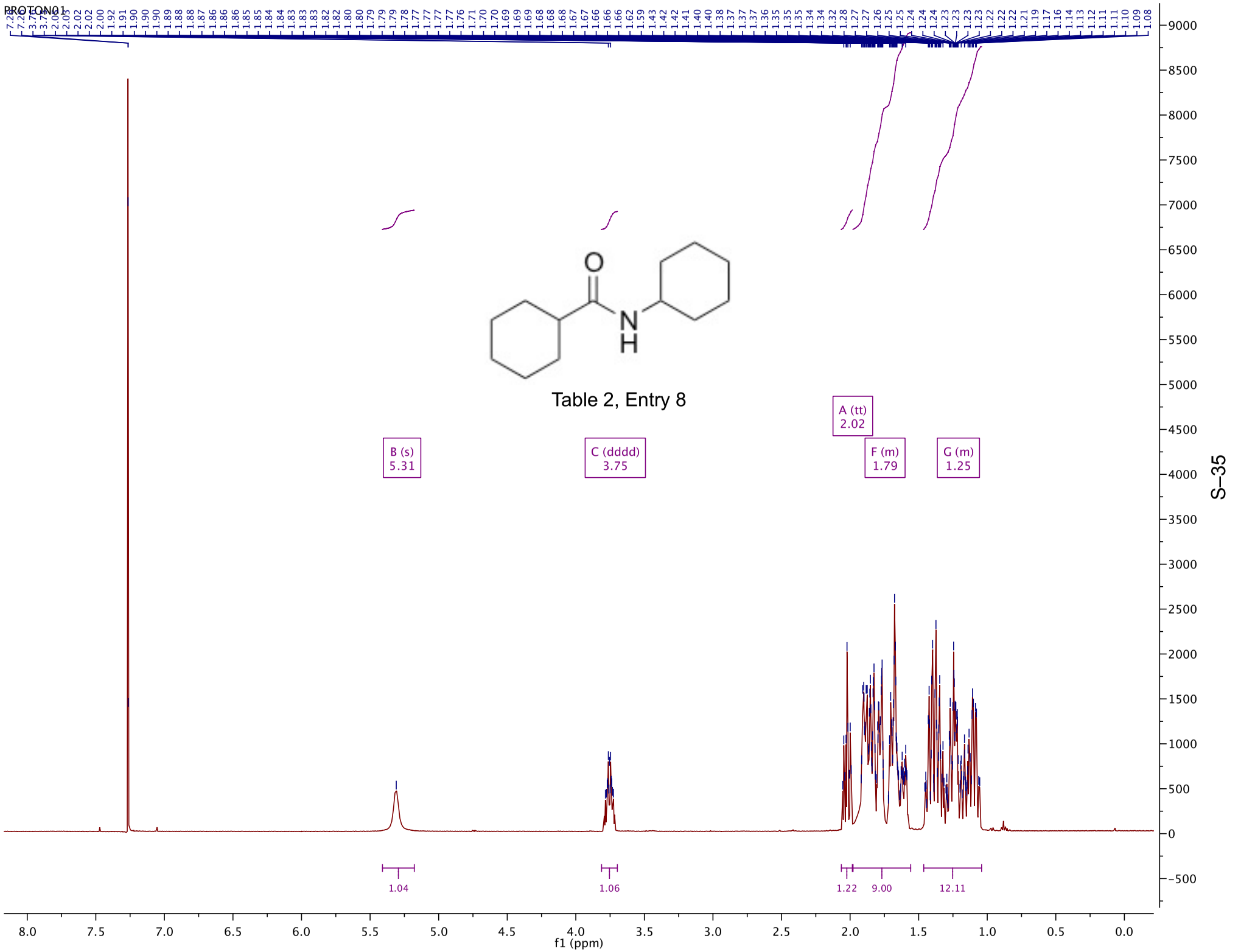
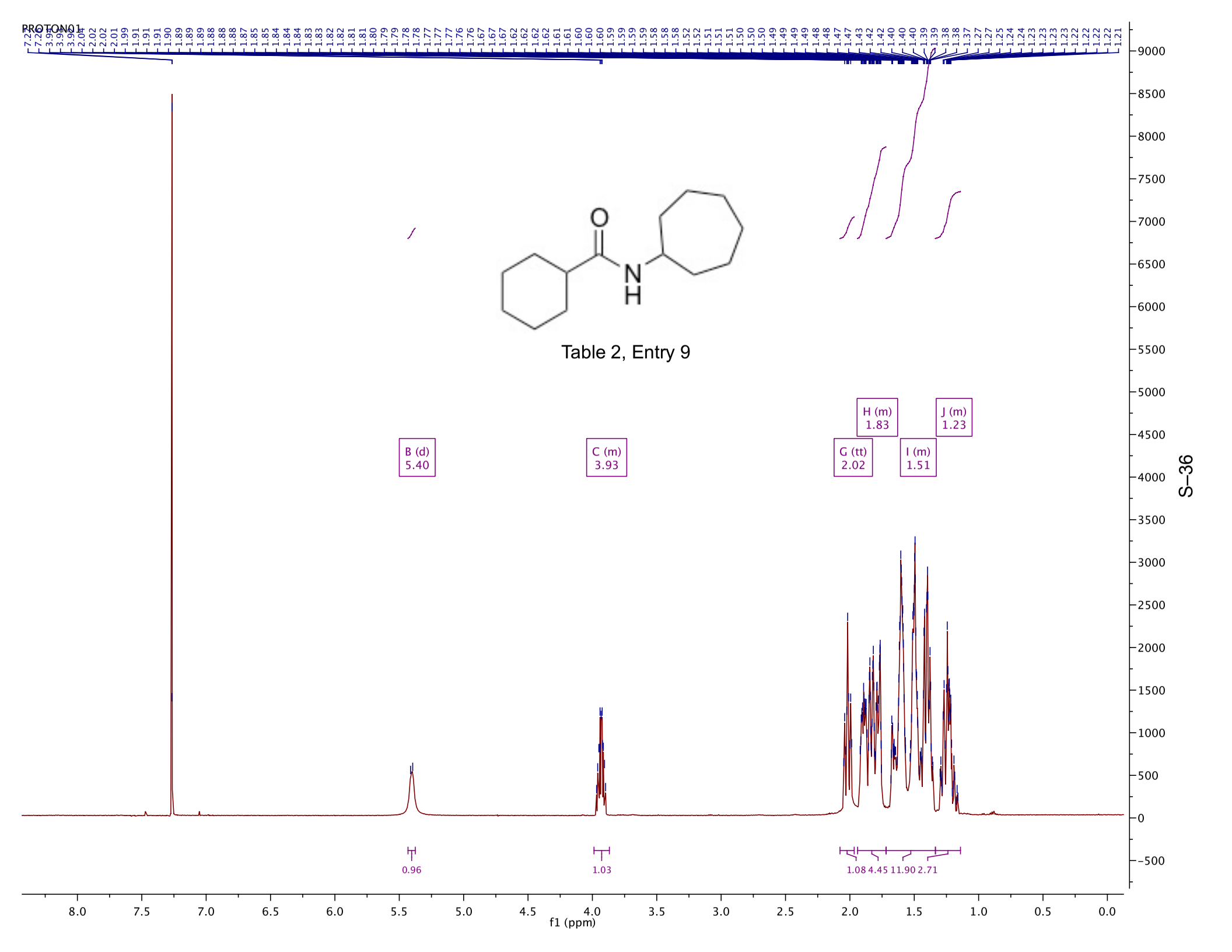
B (m) 7.18
C (d) 5.18
D (dh) 4.06
E (dd) 2.64
F (tt) 2.00
G (m) 1.74
I (qd) 1.41
J (m) 1.20
2.82 3.28
1.10
1.14
2.39
1.04
6.51
2.00 5.08
f1 (ppm)
S–31

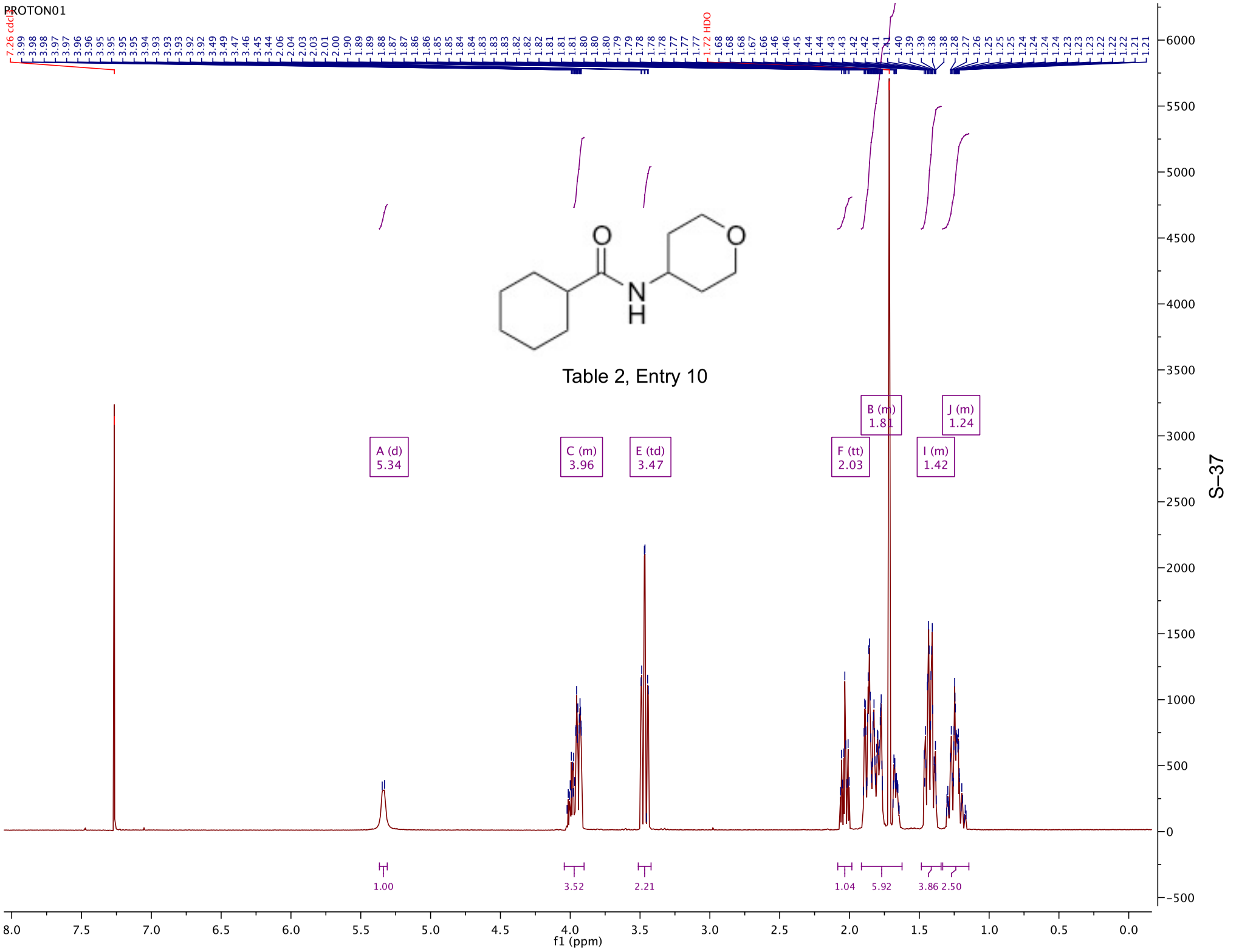

PROTON01
7.27 cdcl3
1.59 HDO
O
Me
N
H
O
Ph
Table 2, Entry 5
A (m) 7.30
C (m) 6.94
D (d) 5.71
E (m) 4.39
F (m) 3.95
G (tt) 2.06
H (m) 1.83
I (ddt) 1.67
K (m) 1.43
L (m) 1.28
2.12
3.11
1.02
0.81
2.27
1.08
3.94
1.05
1.77
5.78
f1 (ppm)
S–32

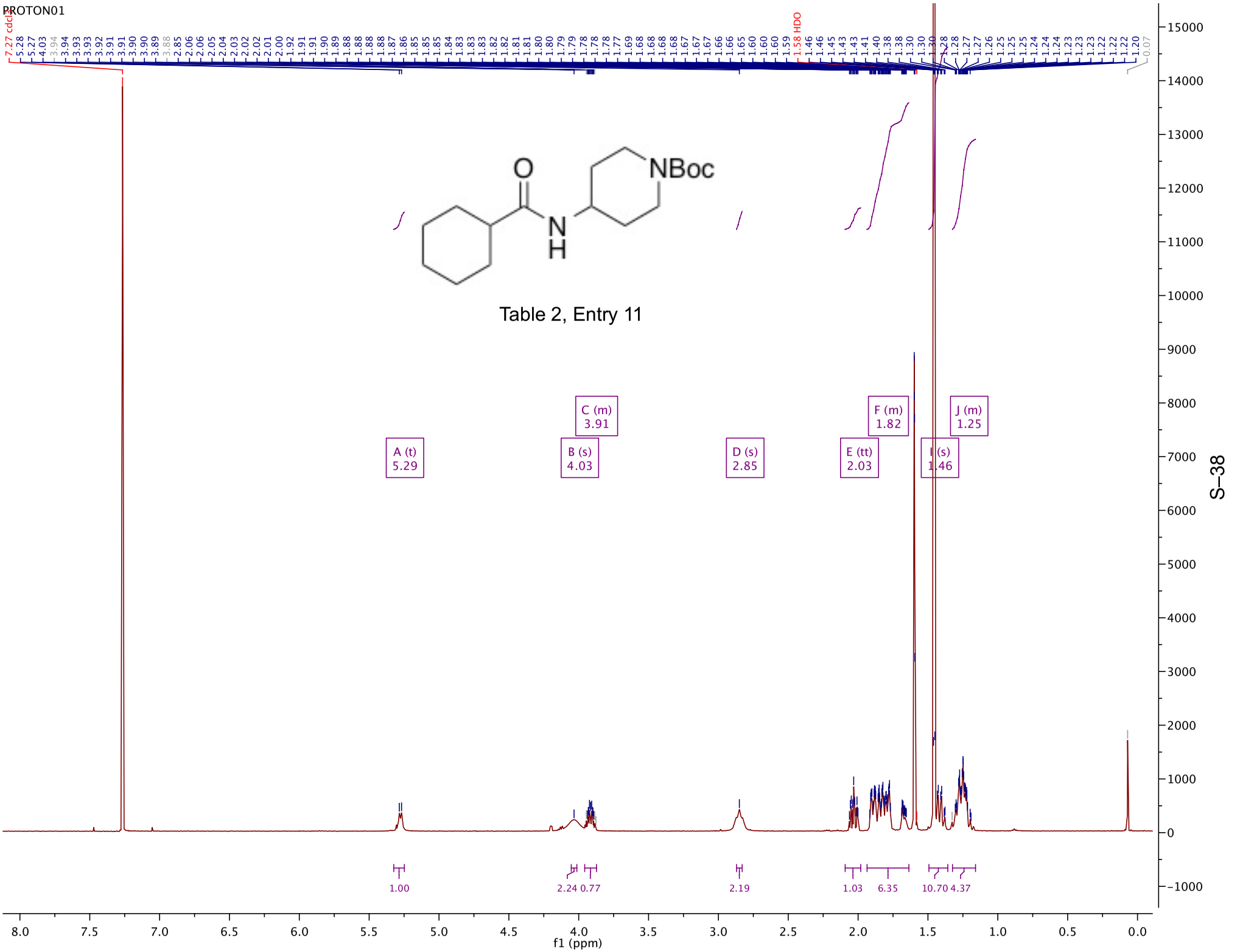

PROTON01
O
Me
O
N
H
O*i*-Pr
Table 2, Entry 6
C (hept)
4.99
B (d)
5.27
D (m)
3.98
G (tt)
2.02
I (m)
1.63
K (m)
1.23
F (m)
2.27
H (m)
1.81
J (m)
1.43
L (d)
1.11
0.99
0.95
1.07
2.11 1.04 4.12 2.55 4.07 9.06 2.99
f1 (ppm)

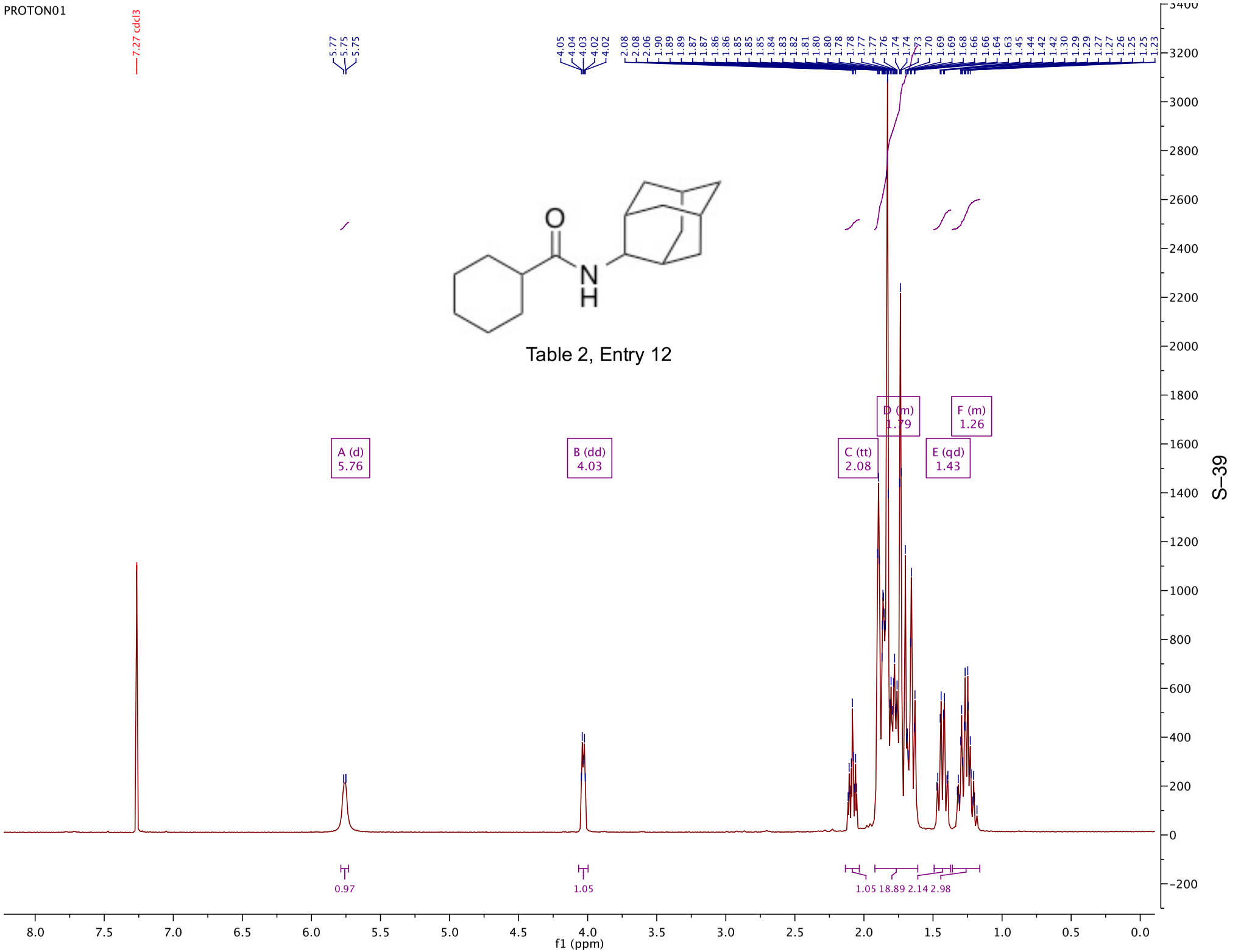

PROTON01
O
Me
N
H
CN
Table 2, Entry 7
D (d)
5.26
E (tddd)
4.08
F (m)
2.37
G (tt)
2.06
H (m)
1.79
J (m)
1.42
K (m)
1.22
1.04
1.01
2.08
1.05
6.96
2.01
5.81
f1 (ppm)

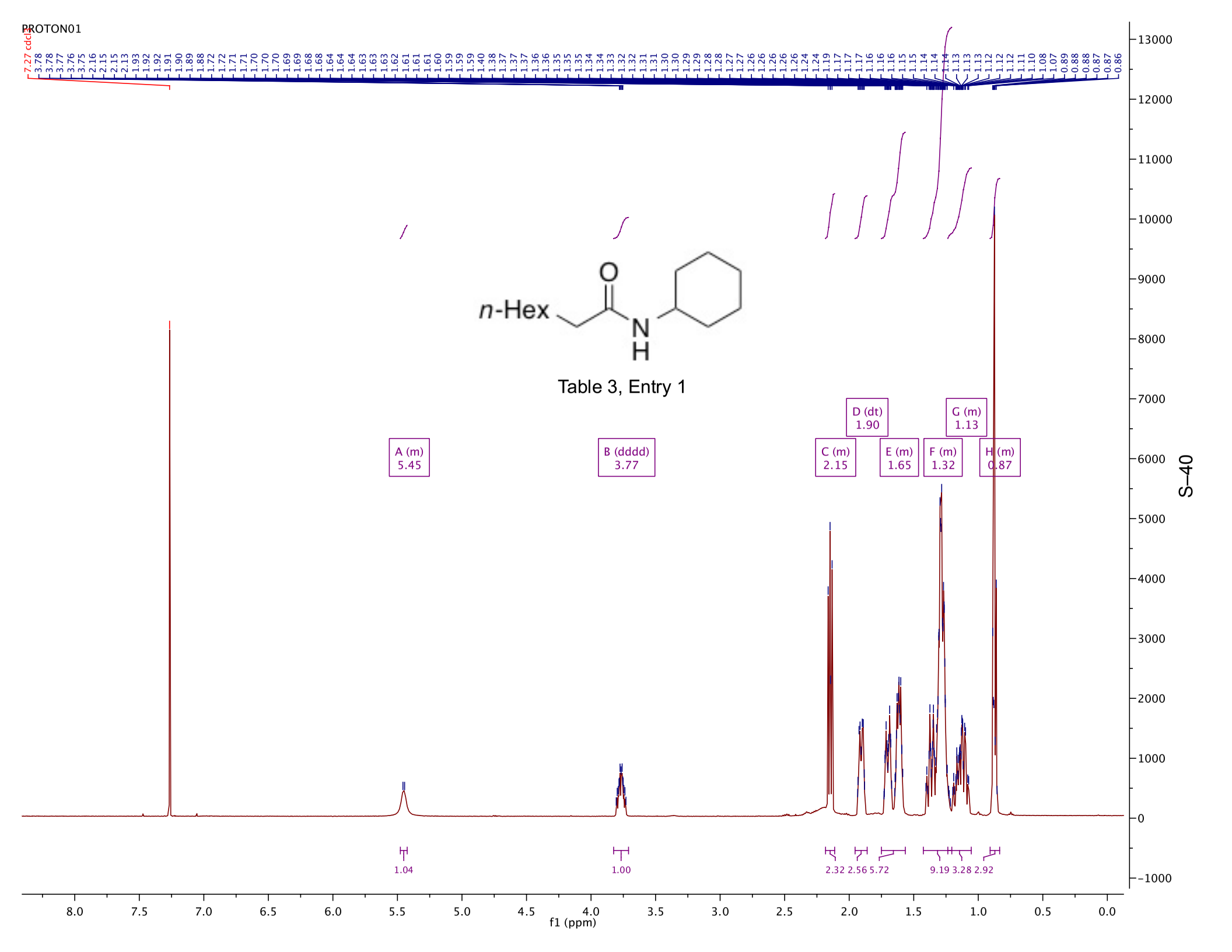

PROTON01
O
N
H
Table 2, Entry 8
B (s)
5.31
C (dddd)
3.75
A (tt)
2.02
F (m)
1.79
G (m)
1.25
1.04
1.06
1.22
9.00
12.11
f1 (ppm)

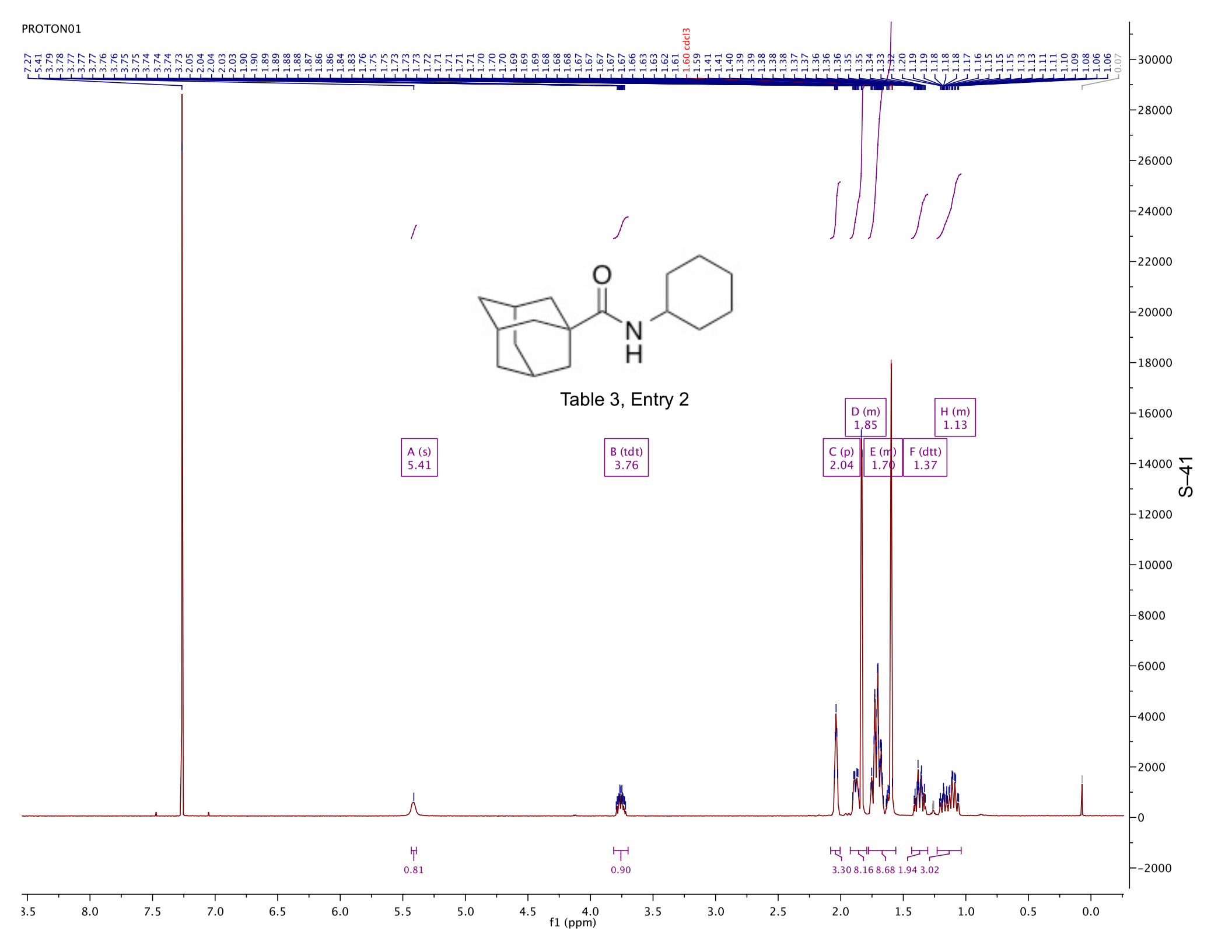

PROTON01
O
N
H
Table 2, Entry 9
B (d)
5.40
C (m)
3.93
G (tt)
2.02
H (m)
1.83
I (m)
1.51
J (m)
1.23
0.96
1.03
1.08 4.45 11.90 2.71
f1 (ppm)

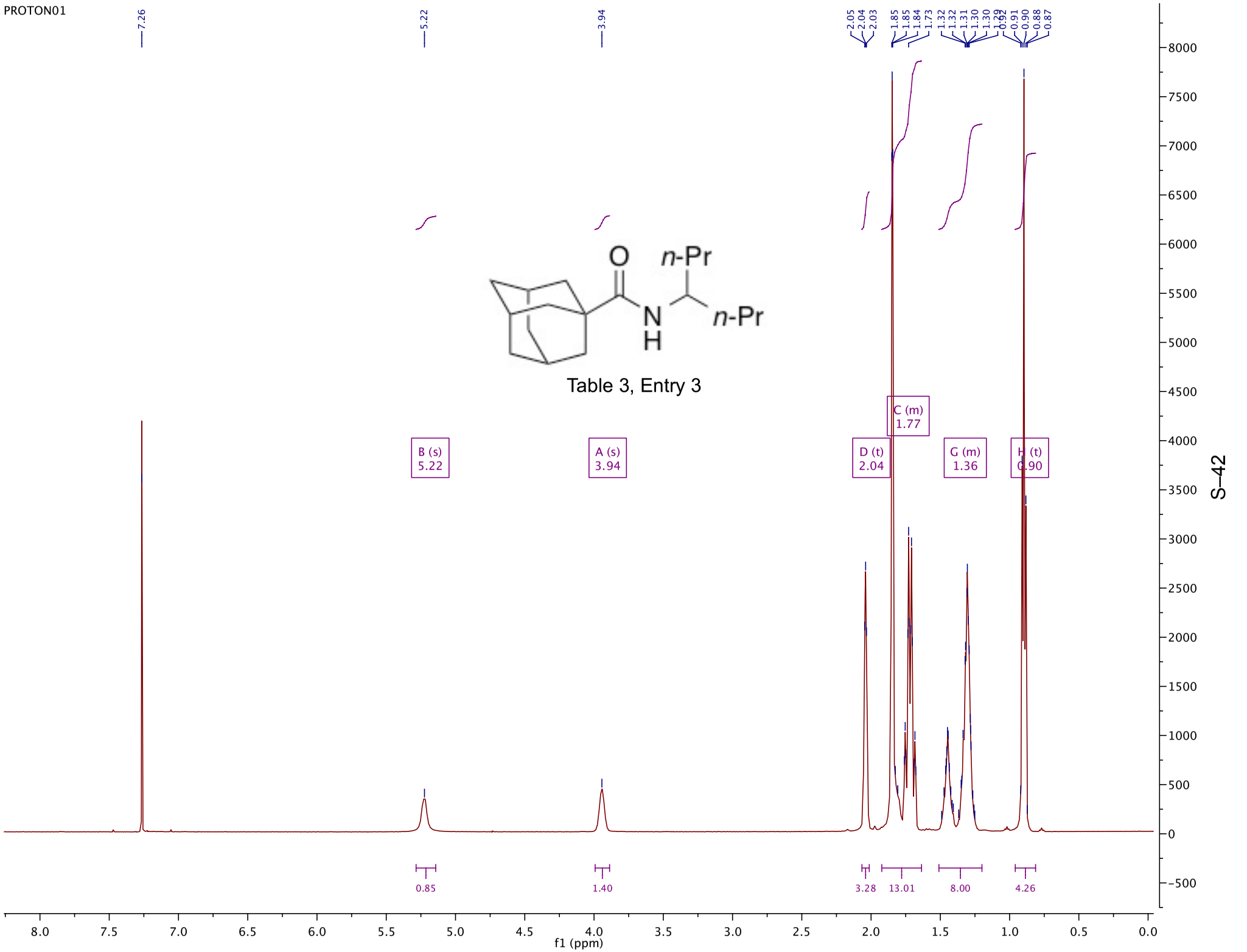

PROTON01
Table 2, Entry 10
A (d) 5.34
C (m) 3.96
E (td) 3.47
F (tt) 2.03
B (m) 1.81
I (m) 1.42
J (m) 1.24
1.00
3.52
2.21
1.04
5.92
3.86
2.50
f1 (ppm)


PROTON01
O
NBoc
N
H
Table 2, Entry 11
A (t)
5.29
B (s)
4.03
C (m)
3.91
D (s)
2.85
E (tt)
2.03
F (m)
1.82
I (s)
1.46
J (m)
1.25
1.00
2.24 0.77
2.19
1.03
6.35
10.70 4.37
f1 (ppm)


PROTON01
7.27 cdcl3
5.77 5.75 5.75
4.05 4.04 4.03 4.02 4.02
2.08 2.08 2.06 1.90 1.89 1.89 1.87 1.87 1.86 1.86 1.85 1.85 1.85 1.84 1.83 1.82 1.81 1.80 1.80 1.78 1.78 1.77 1.77 1.76 1.74 1.74 1.73 1.70 1.69 1.69 1.68 1.66 1.66 1.64 1.63 1.45 1.44 1.42 1.42 1.30 1.29 1.29 1.27 1.27 1.26 1.25 1.25 1.23
O
N
H
Table 2, Entry 12
A (d) 5.76
B (dd) 4.03
C (tt) 2.08
D (m) 1.79
E (qd) 1.43
F (m) 1.26
0.97
1.05
1.05 18.89 2.14 2.98
f1 (ppm)
S–39


PROTON01
n-Hex
O
N
H
Table 3, Entry 1
A (m) 5.45
B (dddd) 3.77
C (m) 2.15
D (dt) 1.90
E (m) 1.65
F (m) 1.32
G (m) 1.13
H (m) 0.87
1.04
1.00
2.32 2.56 5.72
9.19 3.28 2.92
f1 (ppm)
S–40


PROTON01
O
N
H
Table 3, Entry 2
A (s)
5.41
B (tdt)
3.76
C (p)
2.04
D (m)
1.85
E (m)
1.70
F (dtt)
1.37
H (m)
1.13
0.81
0.90
3.30 8.16 8.68 1.94 3.02
f1 (ppm)
S–41


PROTON01
7.26
5.22
3.94
2.05
2.04
2.03
1.85
1.85
1.84
1.73
1.32
1.32
1.31
1.30
1.30
0.92
0.91
0.90
0.88
0.87
O
n-Pr
N
H
n-Pr
Table 3, Entry 3
B (s)
5.22
A (s)
3.94
C (m)
1.77
D (t)
2.04
G (m)
1.36
H (t)
0.90
0.85
1.40
3.28
13.01
8.00
4.26
f1 (ppm)
S–42

PROTON01

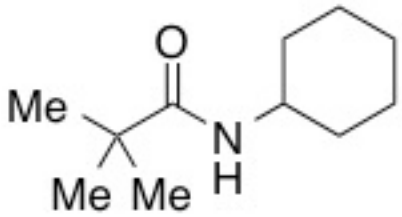


Table 3, Entry 4

A (s) 5.44

B (m) 3.74

C (m) 1.89

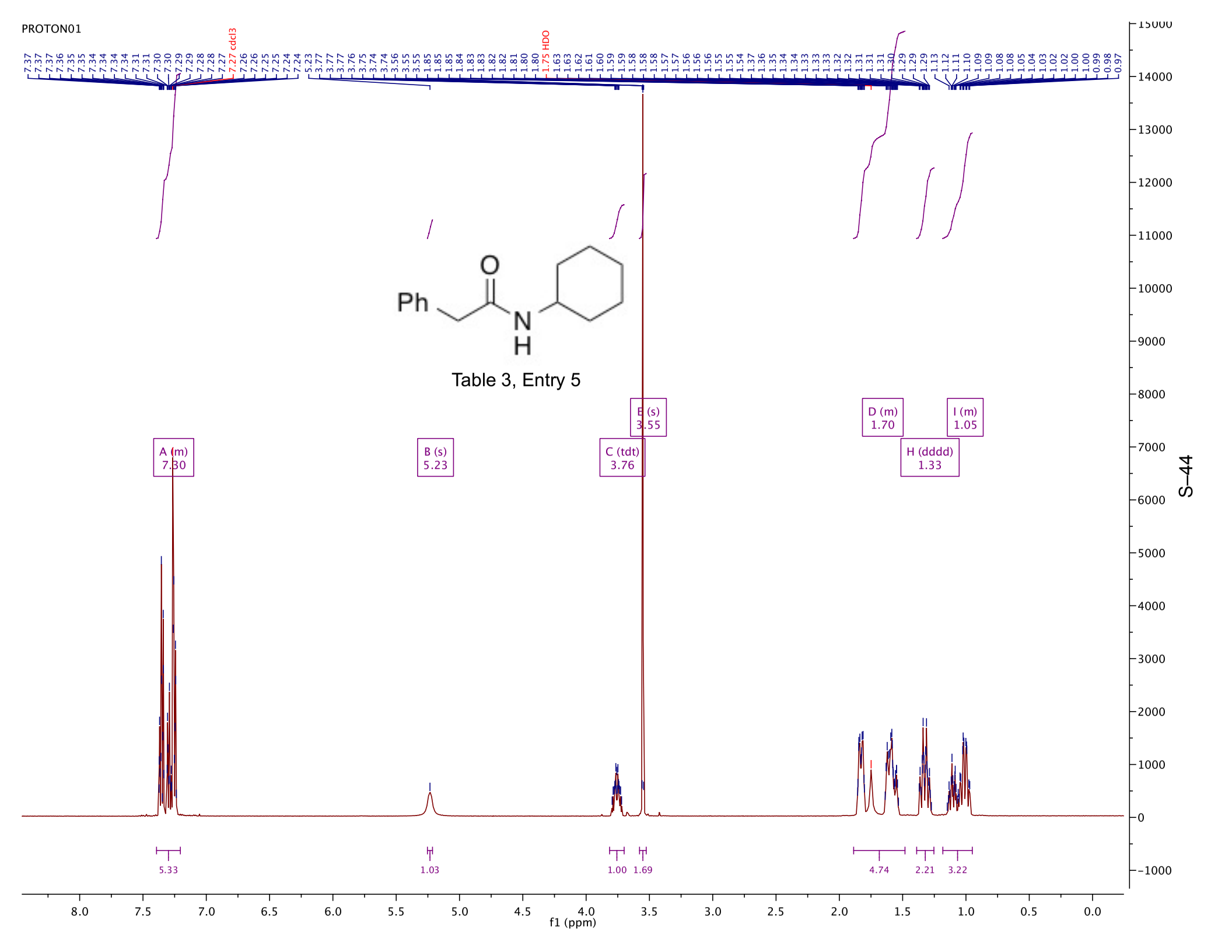
D (m) 1.66

E (dtt) 1.37

F (s) 1.18

1.05 0.81 2.04 2.73 2.20 11.25

f1 (ppm)


PROTON01
7.27 cdcl3
1.75 HDO
O
Ph
N
H
Table 3, Entry 5
A (m)
7.30
B (s)
5.23
C (tdt)
3.76
E (s)
3.55
D (m)
1.70
H (dddd)
1.33
I (m)
1.05
5.33
1.03
1.00
1.69
4.74
2.21
3.22
f1 (ppm)
S–44

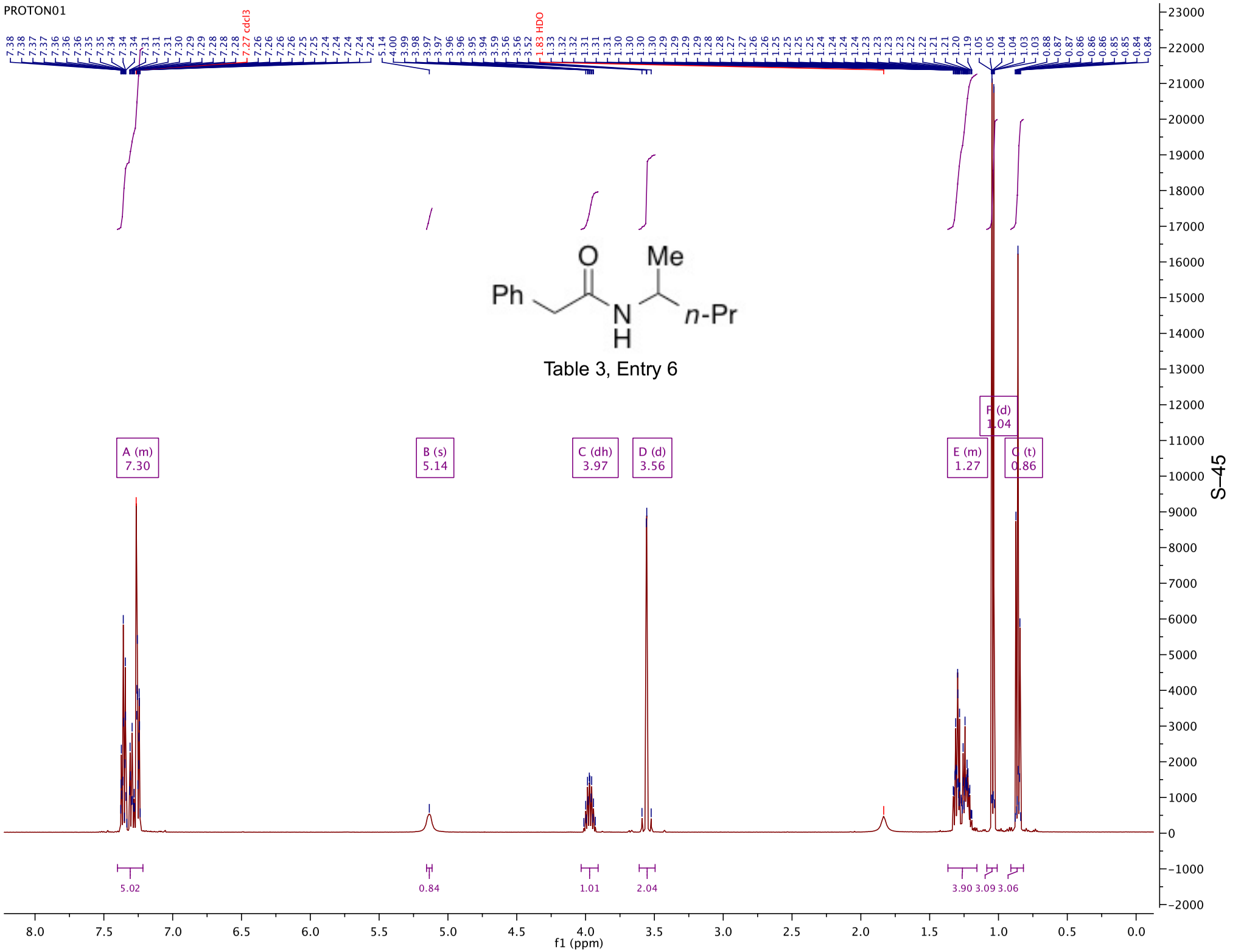
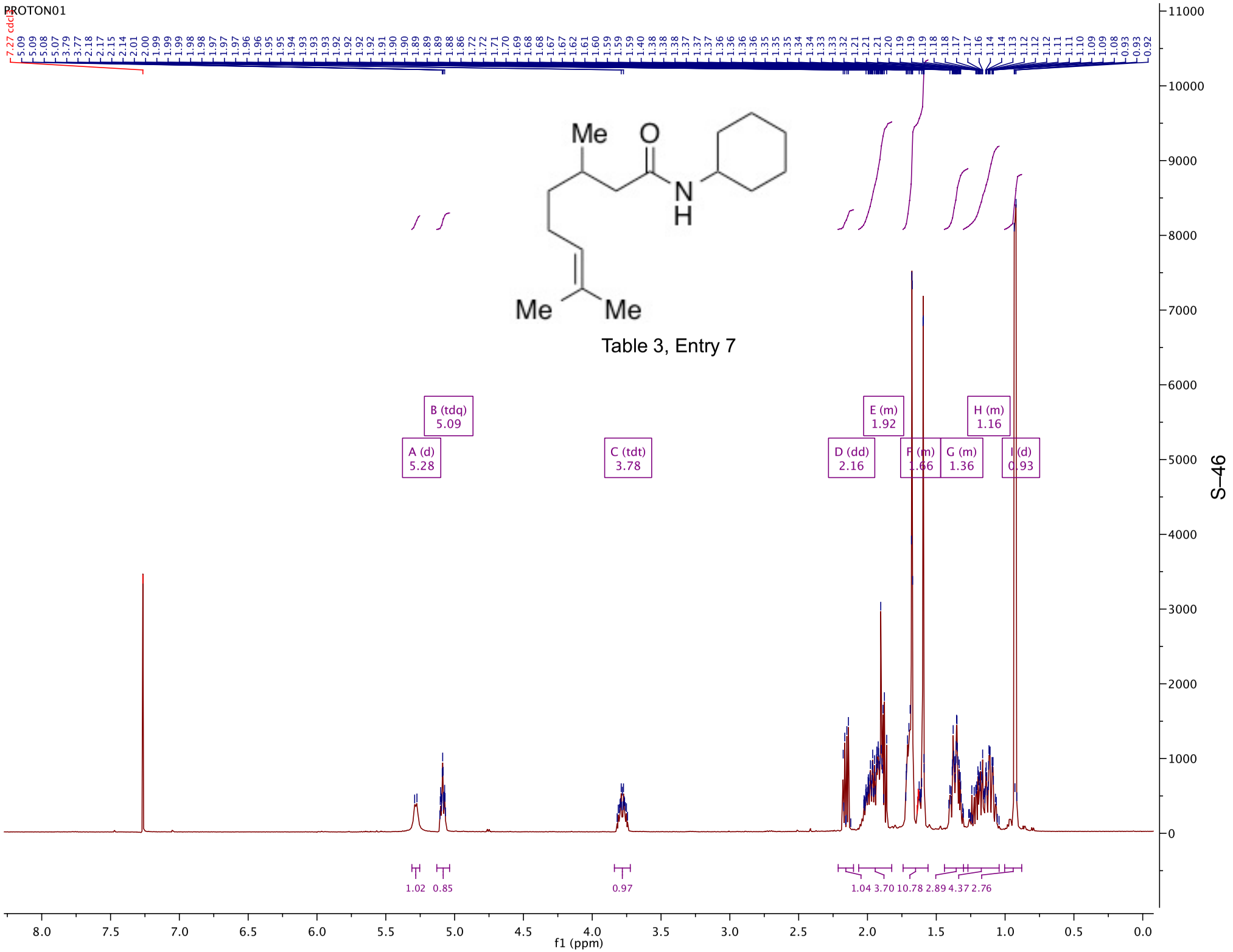
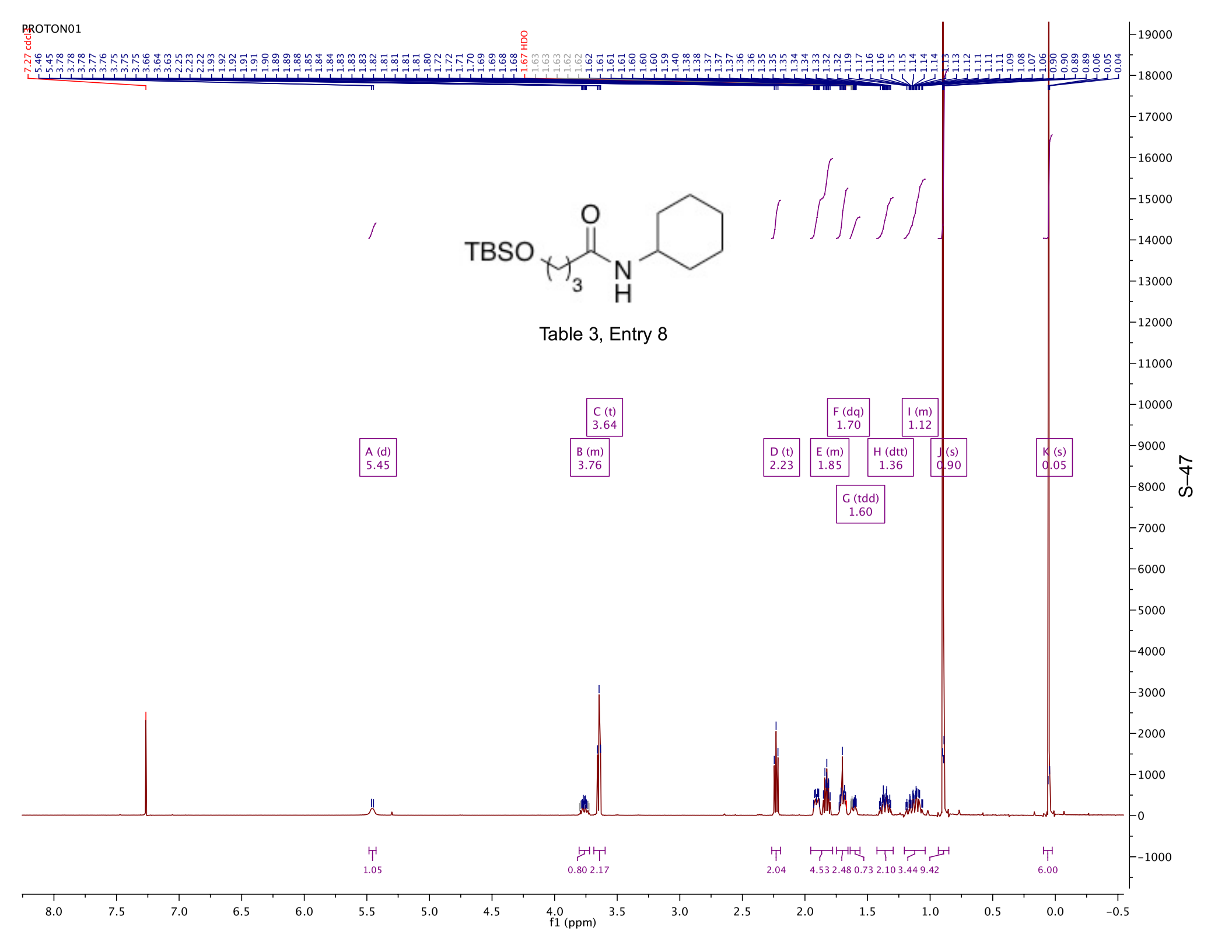
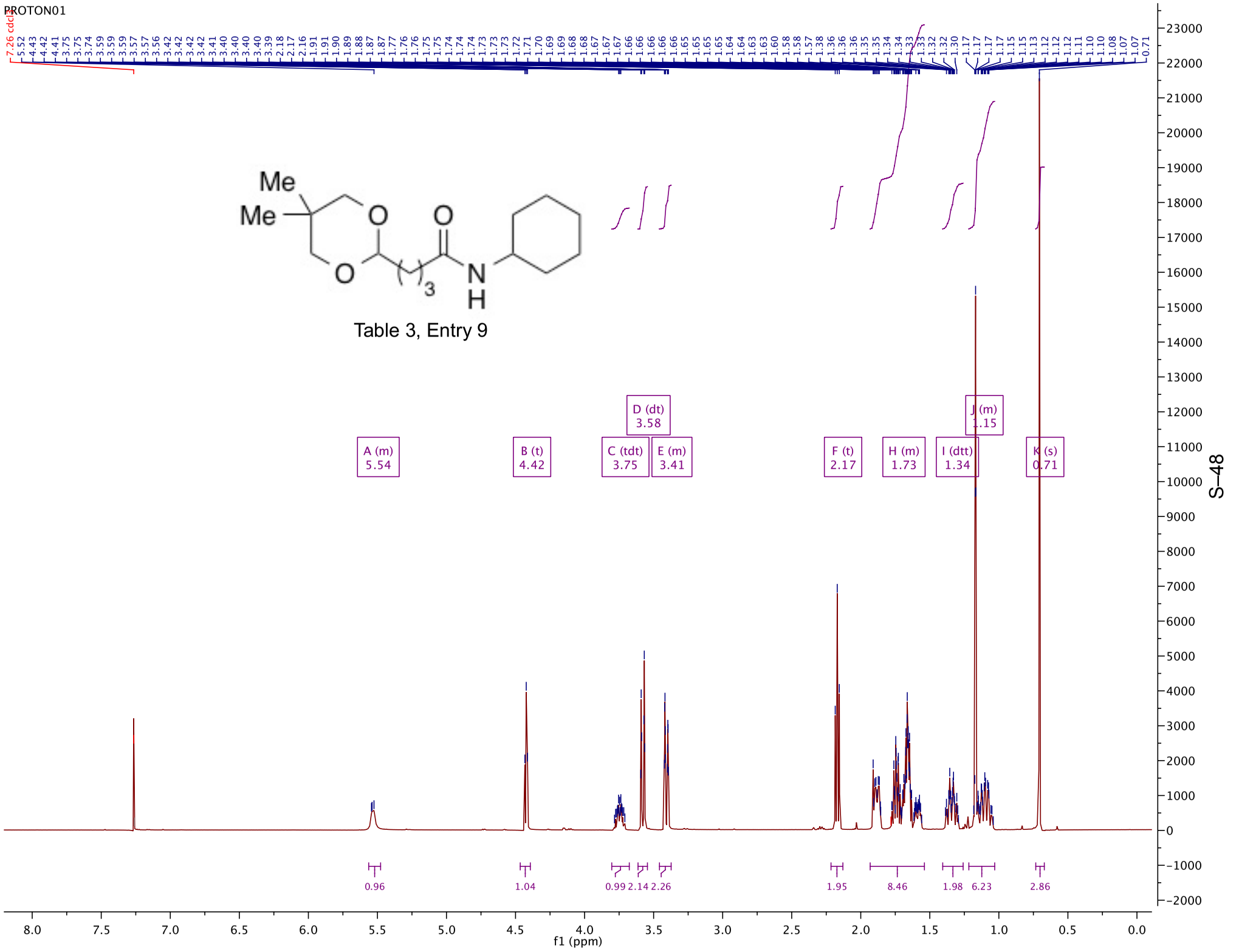
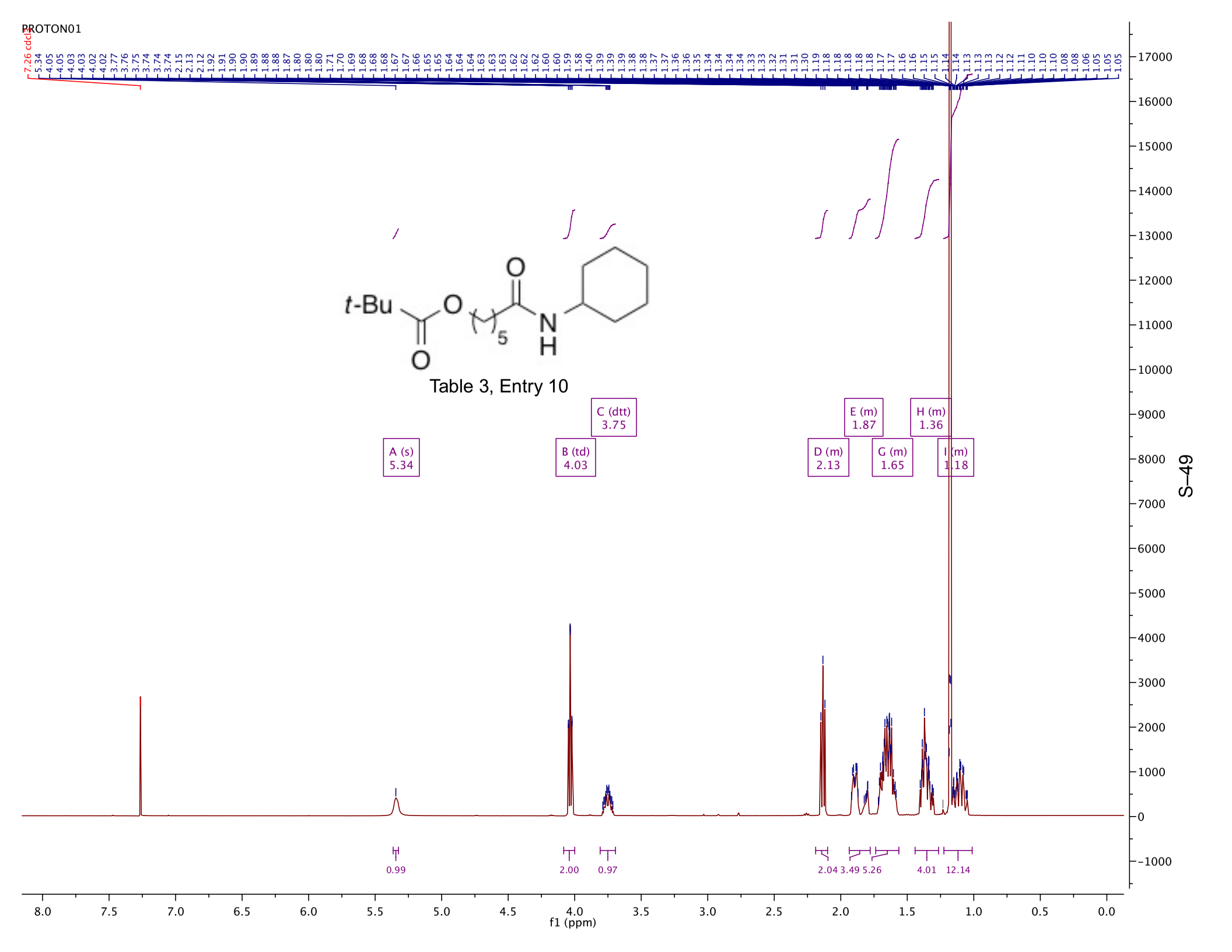


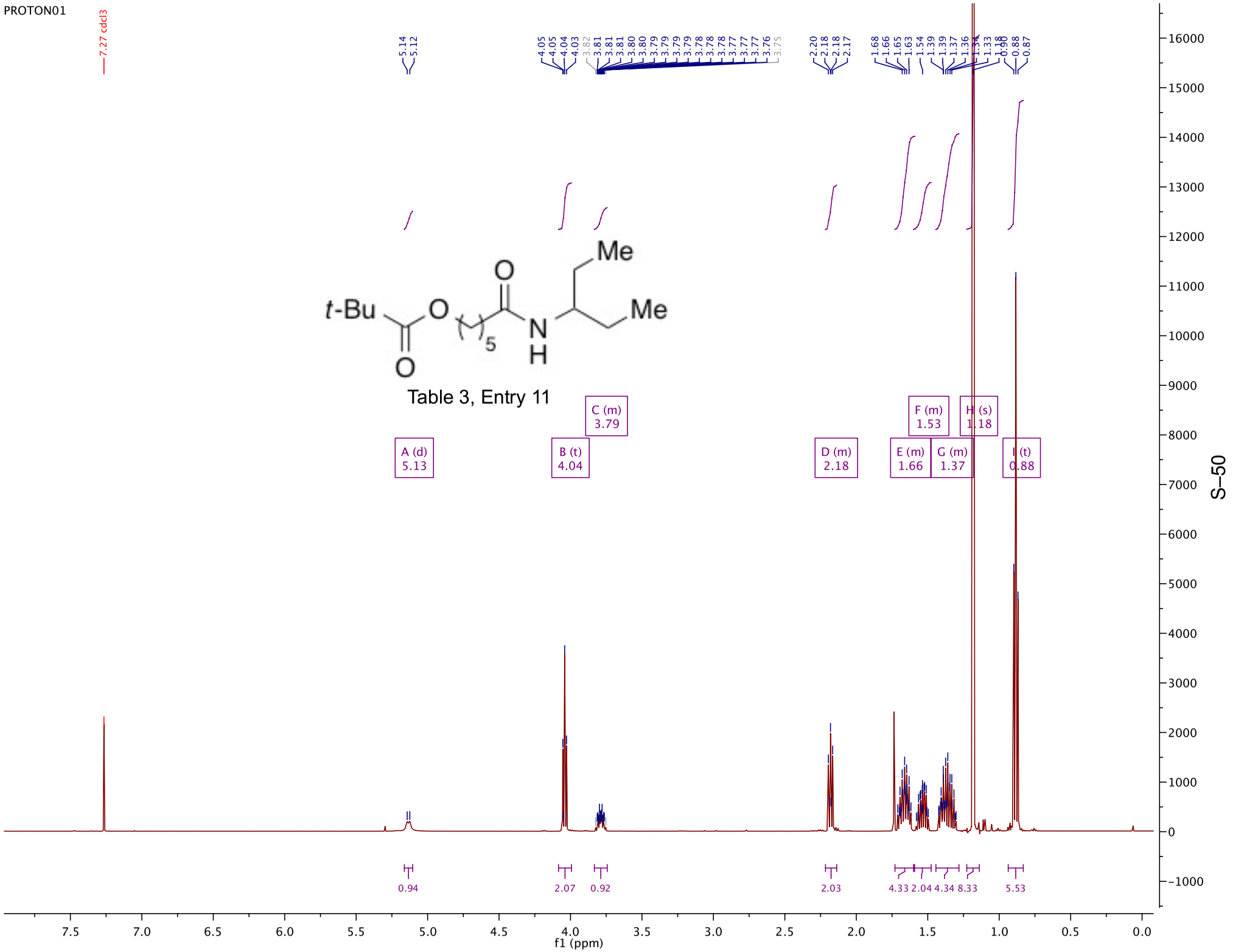
Table 3, Entry 6

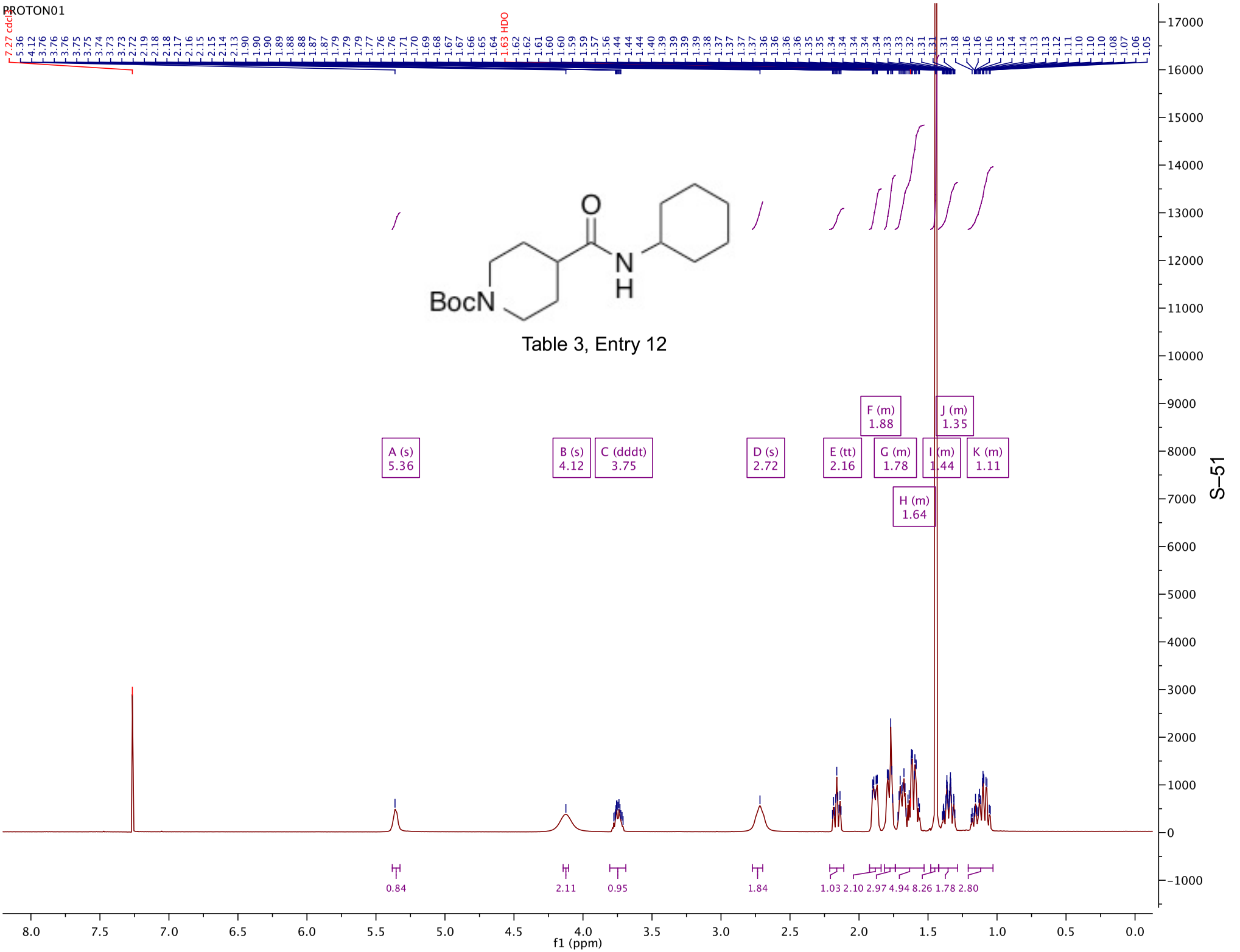

PROTON01
Me
O
N
H
Me
Me
Table 3, Entry 7
A (d)
5.28
B (tdq)
5.09
C (tdt)
3.78
D (dd)
2.16
E (m)
1.92
F (m)
1.66
G (m)
1.36
H (m)
1.16
I (d)
0.93
1.02
0.85
0.97
1.04
3.70
10.78
2.89
4.37
2.76
f1 (ppm)


PROTON01
TBSO
O
N
H
3
Table 3, Entry 8
A (d) 5.45
B (m) 3.76
C (t) 3.64
D (t) 2.23
E (m) 1.85
F (dq) 1.70
G (tdd) 1.60
H (dtt) 1.36
I (m) 1.12
J (s) 0.90
K (s) 0.05
1.05
0.80 2.17
2.04
4.53 2.48 0.73 2.10 3.44 9.42
6.00
f1 (ppm)
S–47


PROTON01
Me
Me
O
O
O
3
N
H
Table 3, Entry 9
A (m) 5.54
B (t) 4.42
D (dt) 3.58
C (tdt) 3.75
E (m) 3.41
F (t) 2.17
H (m) 1.73
I (dtt) 1.34
J (m) 1.15
K (s) 0.71
0.96
1.04
0.99 2.14 2.26
1.95
8.46
1.98 6.23
2.86
f1 (ppm)
S–48


PROTON01
t-Bu
O
O
O
N
H
5
Table 3, Entry 10
A (s)
5.34
B (td)
4.03
C (dtt)
3.75
D (m)
2.13
E (m)
1.87
G (m)
1.65
H (m)
1.36
I (m)
1.18
0.99
2.00
0.97
2.04
3.49
5.26
4.01
12.14
f1 (ppm)


PROTON01
7.27 cdcl3
5.14
5.12
4.05
4.05
4.04
4.03
3.82
3.81
3.81
3.81
3.80
3.80
3.79
3.79
3.79
3.79
3.78
3.78
3.78
3.77
3.77
3.77
3.76
3.75
2.20
2.18
2.18
2.17
1.68
1.66
1.65
1.63
1.54
1.39
1.39
1.37
1.36
1.34
1.33
1.18
0.90
0.88
0.87
t-Bu
O
O
5
O
N
H
Me
Me
Table 3, Entry 11
A (d)
5.13
B (t)
4.04
C (m)
3.79
D (m)
2.18
E (m)
1.66
F (m)
1.53
G (m)
1.37
H (s)
1.18
I (t)
0.88
0.94
2.07
0.92
2.03
4.33
2.04
4.34
8.33
5.53
f1 (ppm)
S–50


PROTON01
BocN
O
N
H
Table 3, Entry 12
A (s) 5.36
B (s) 4.12
C (dddt) 3.75
D (s) 2.72
E (tt) 2.16
F (m) 1.88
G (m) 1.78
H (m) 1.64
I (m) 1.44
J (m) 1.35
K (m) 1.11
0.84
2.11
0.95
1.84
1.03 2.10 2.97 4.94 8.26 1.78 2.80
f1 (ppm)

PROTON01

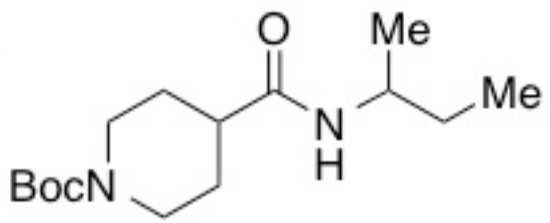
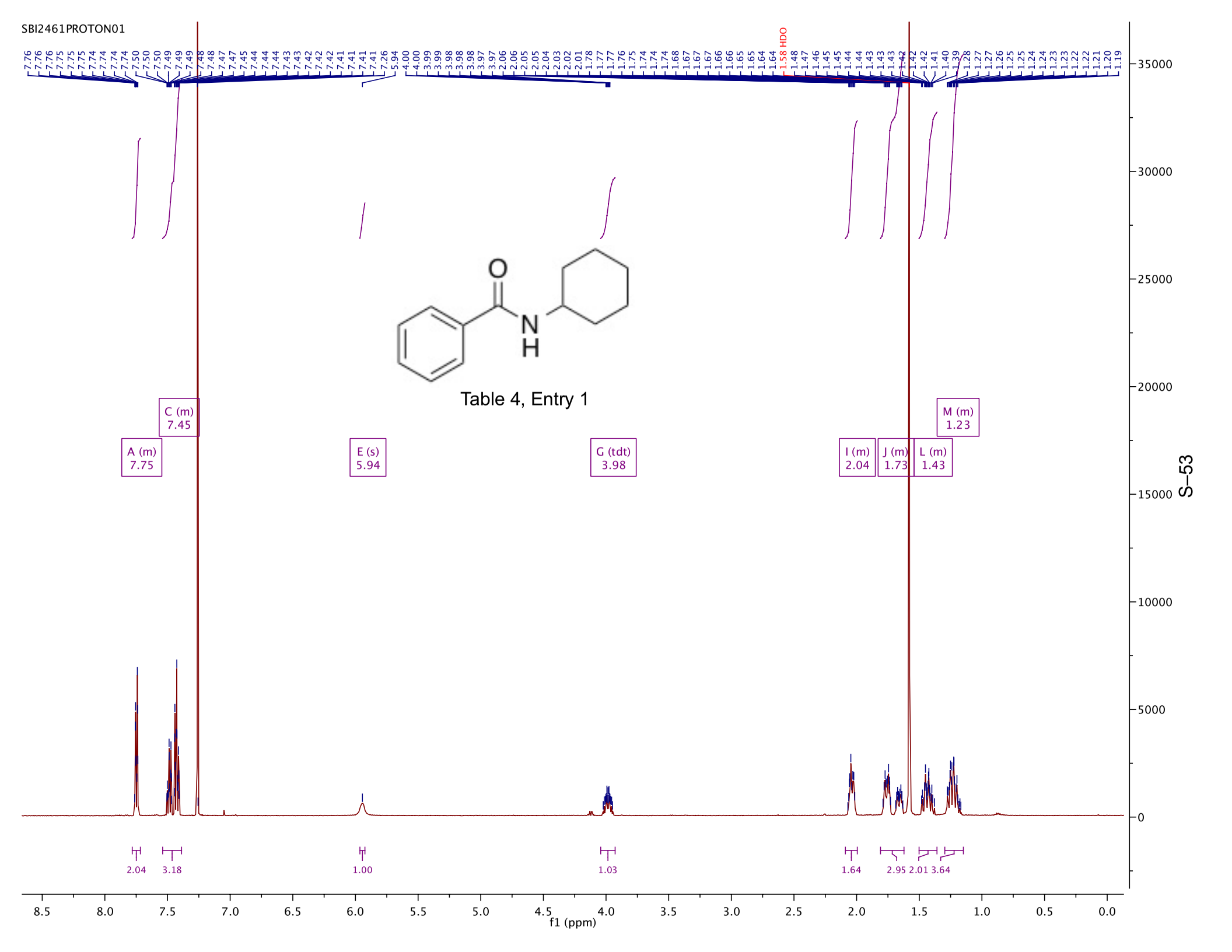
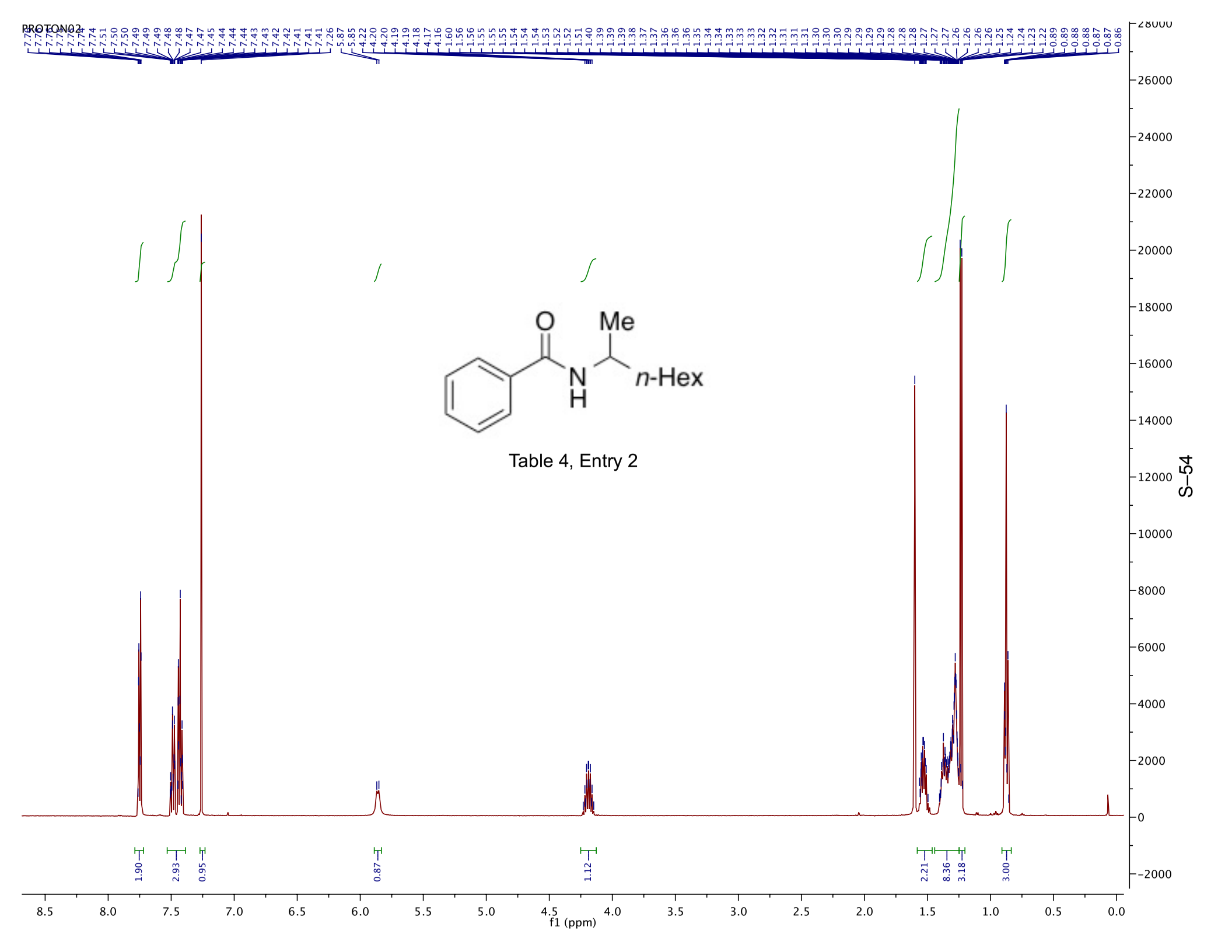
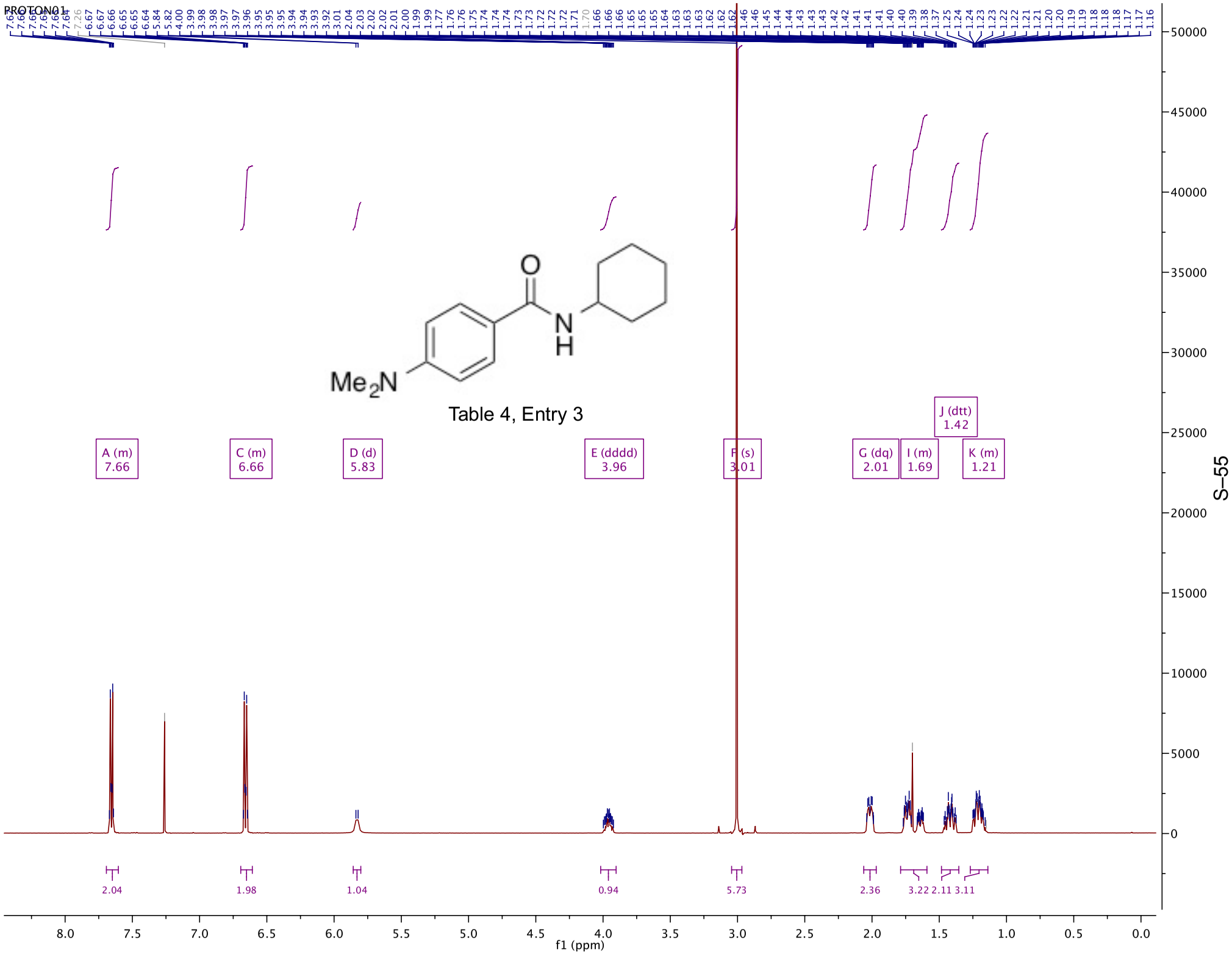
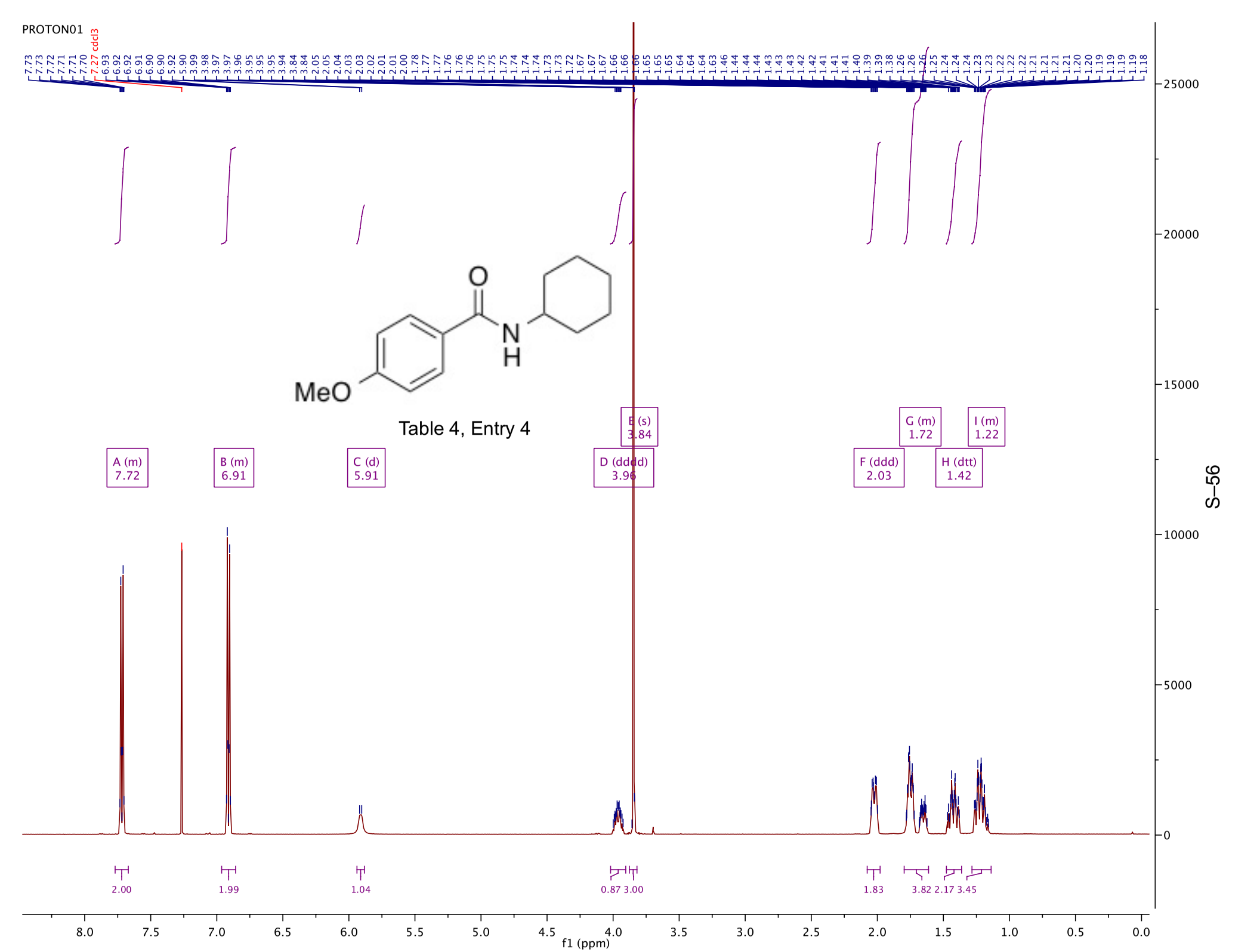


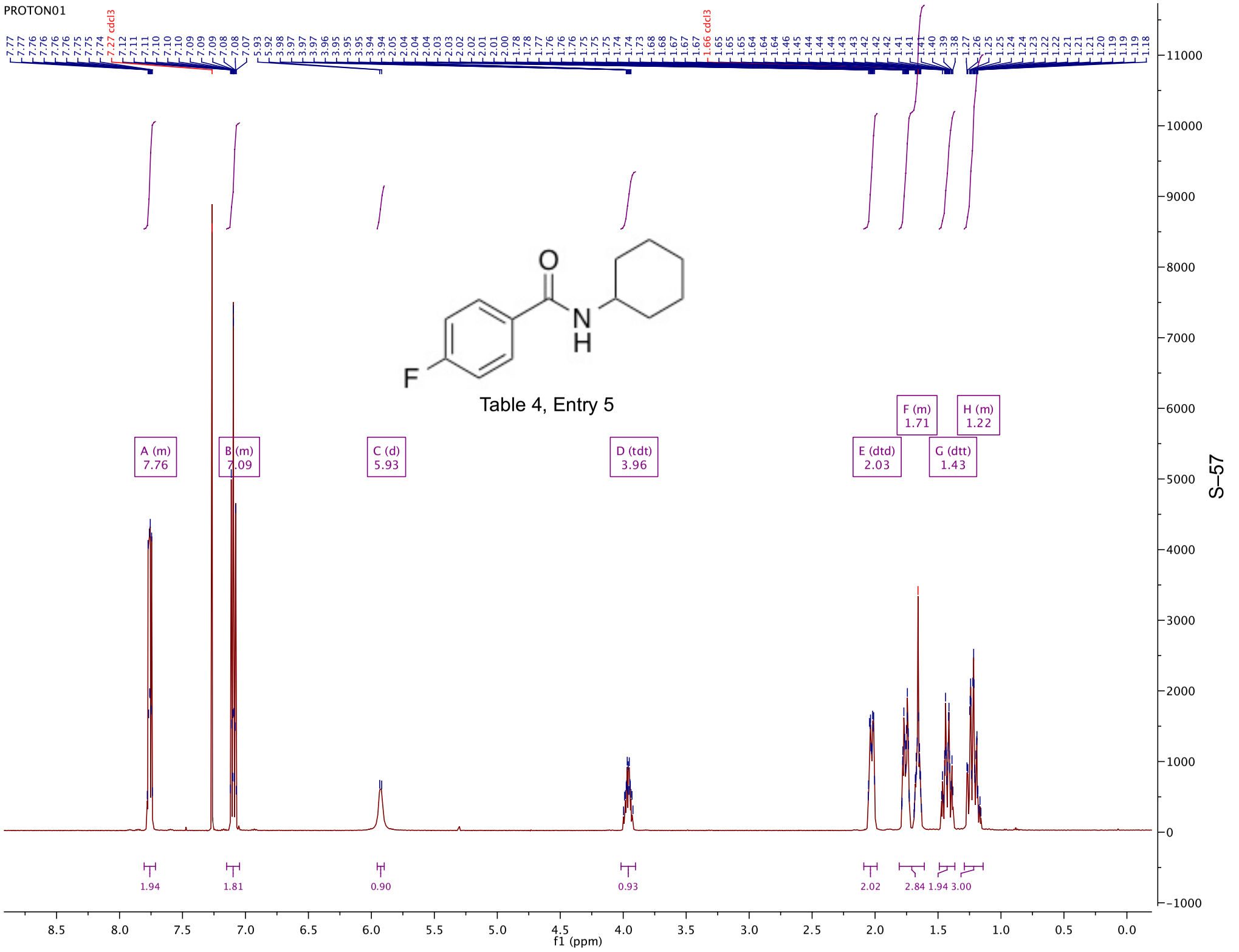
Table 3, Entry 13

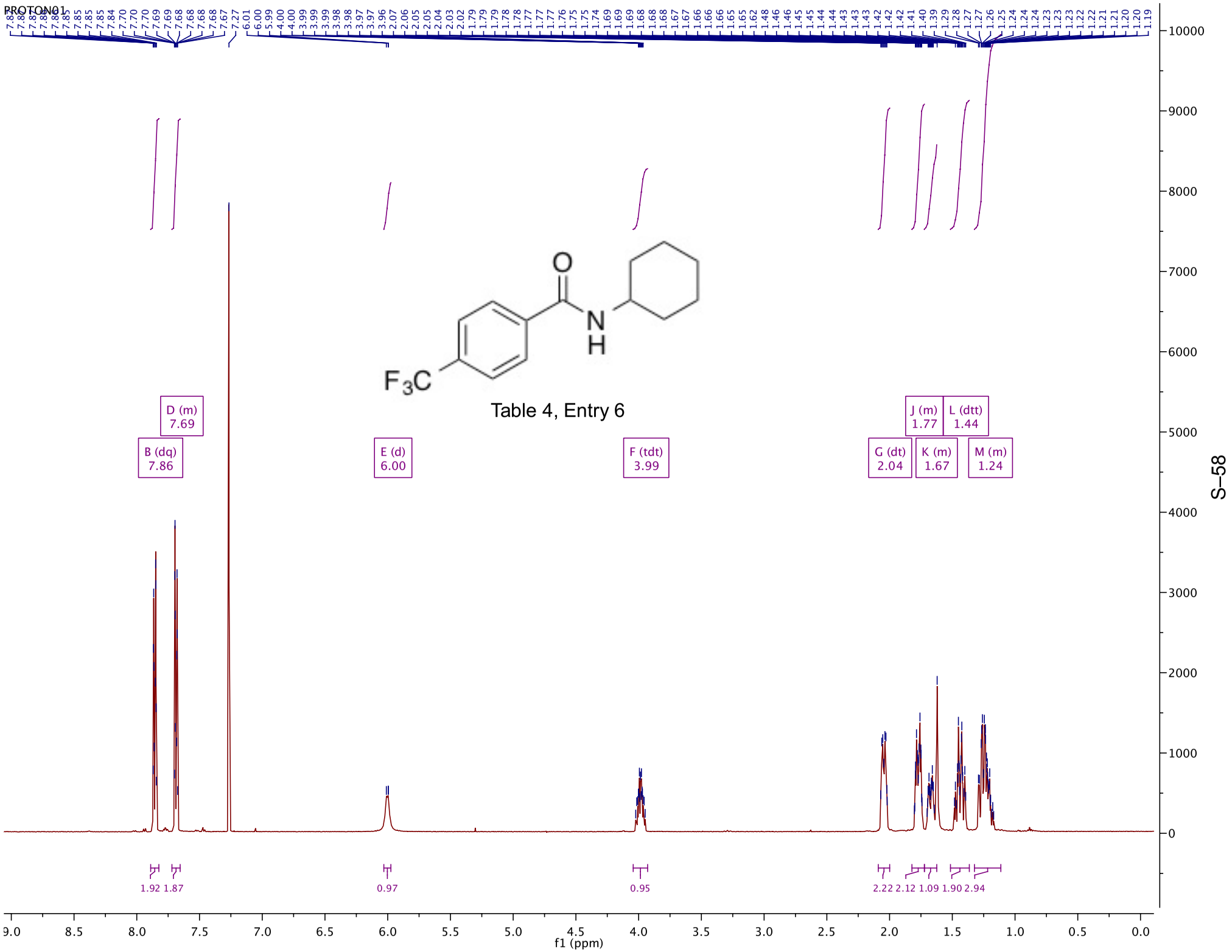

SBI2461PROTON01
HDO
O
N
H
Table 4, Entry 1
A (m) 7.75
C (m) 7.45
E (s) 5.94
G (tdt) 3.98
I (m) 2.04
J (m) 1.73
L (m) 1.43
M (m) 1.23
2.04
3.18
1.00
1.03
1.64
2.95
2.01
3.64
f1 (ppm)

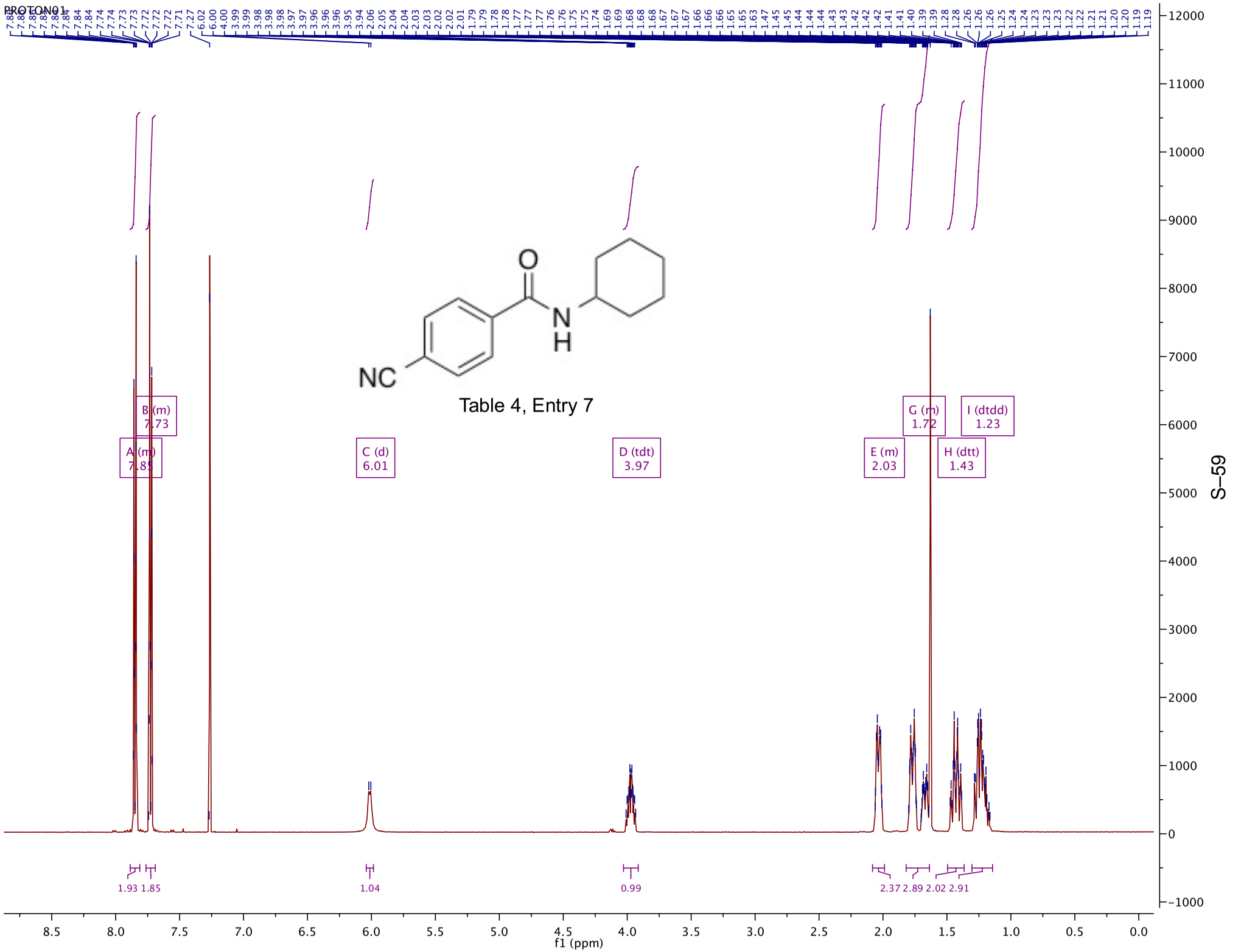

PROTON02
O
Me
N
H
n-Hex
Table 4, Entry 2
f1 (ppm)
S–54

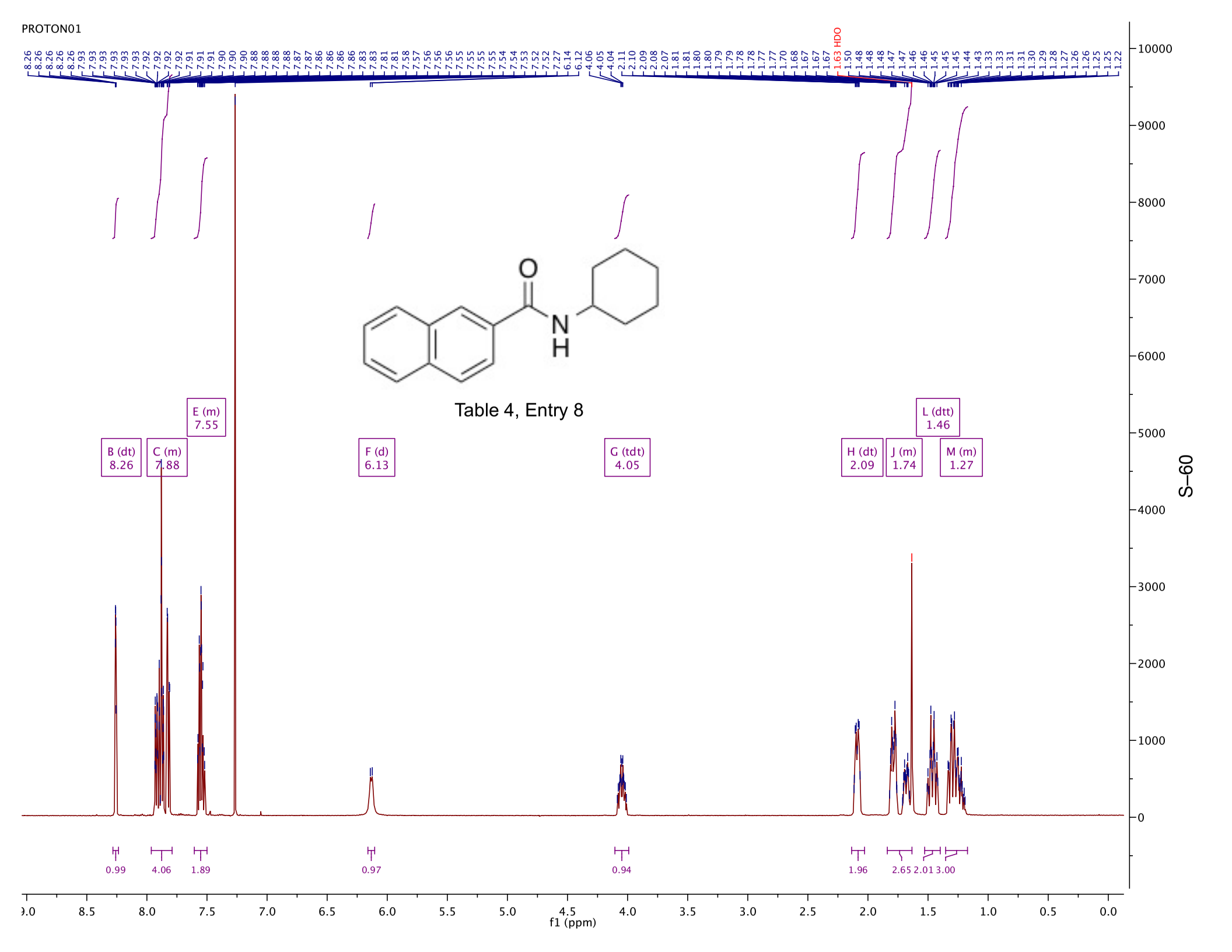

PROTON01
O
N
H
Me2N
Table 4, Entry 3
A (m) 7.66
C (m) 6.66
D (d) 5.83
E (dddd) 3.96
F (s) 3.01
G (dq) 2.01
I (m) 1.69
J (dtt) 1.42
K (m) 1.21
2.04
1.98
1.04
0.94
5.73
2.36
3.22
2.11
3.11
f1 (ppm)

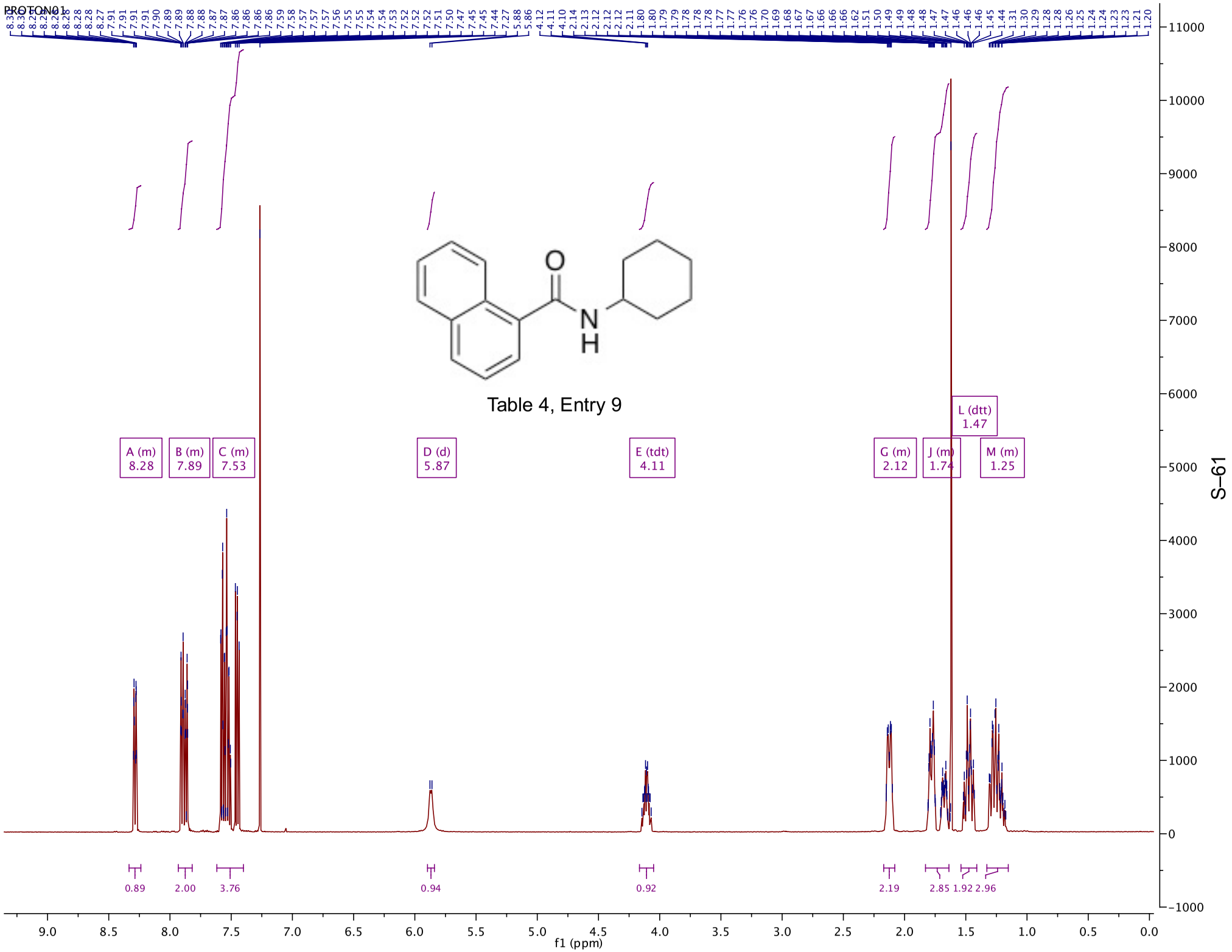

PROTON01
7.27 cdcl3
O
N
H
MeO
Table 4, Entry 4
A (m) 7.72
B (m) 6.91
C (d) 5.91
D (dddd) 3.96
E (s) 3.84
F (ddd) 2.03
G (m) 1.72
H (dtt) 1.42
I (m) 1.22
2.00
1.99
1.04
0.87 3.00
1.83
3.82 2.17 3.45
f1 (ppm)

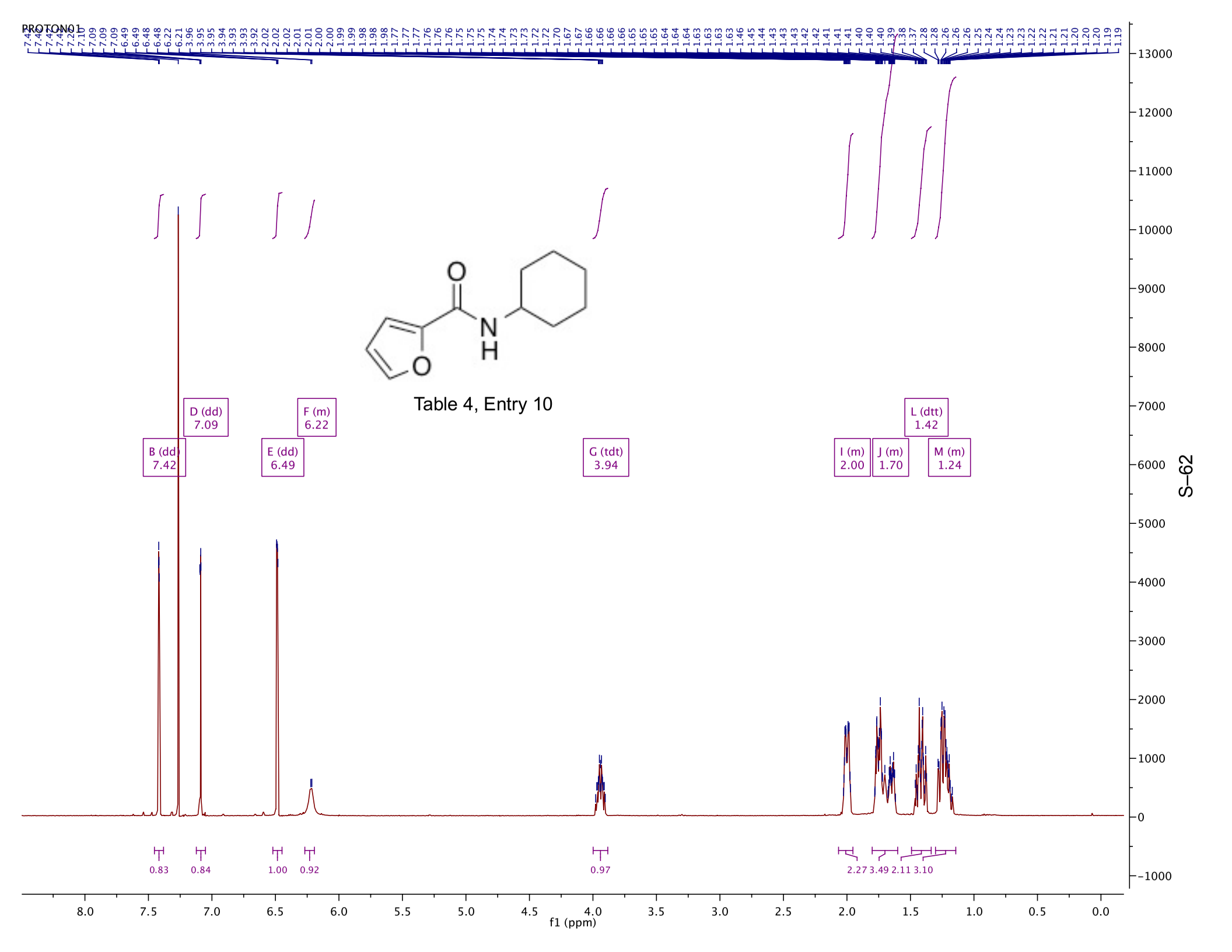

PROTON01
O
N
H
F
Table 4, Entry 5
A (m) 7.76
B (m) 7.09
C (d) 5.93
D (tdt) 3.96
E (dtd) 2.03
F (m) 1.71
G (dtt) 1.43
H (m) 1.22
1.94
1.81
0.90
0.93
2.02
2.84
1.94
3.00
f1 (ppm)

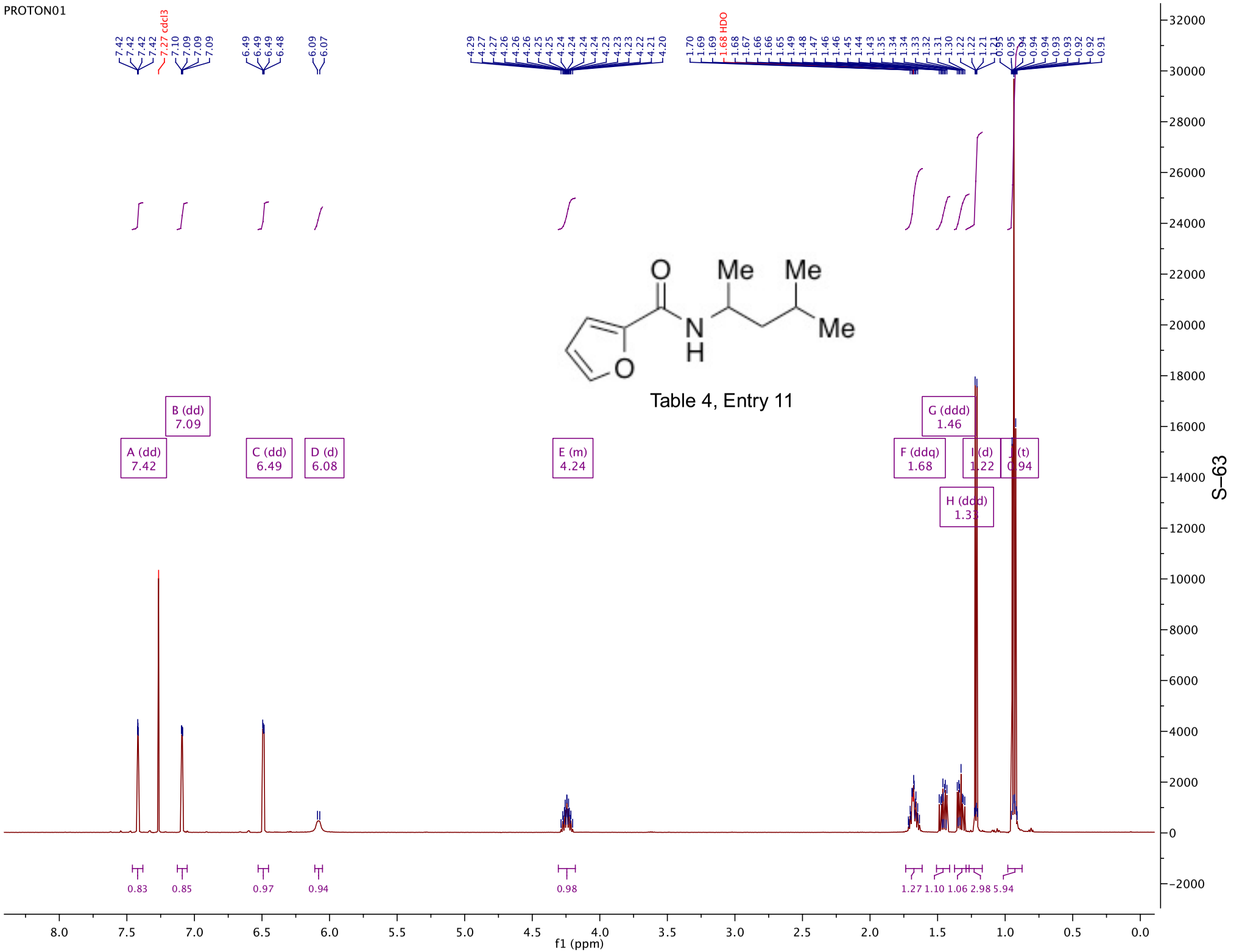

PROTON01
O
N
H
F3C
Table 4, Entry 6
D (m) 7.69
B (dq) 7.86
E (d) 6.00
F (tdt) 3.99
J (m) 1.77
L (dtt) 1.44
G (dt) 2.04
K (m) 1.67
M (m) 1.24
1.92 1.87
0.97
0.95
2.22 2.12 1.09 1.90 2.94
f1 (ppm)

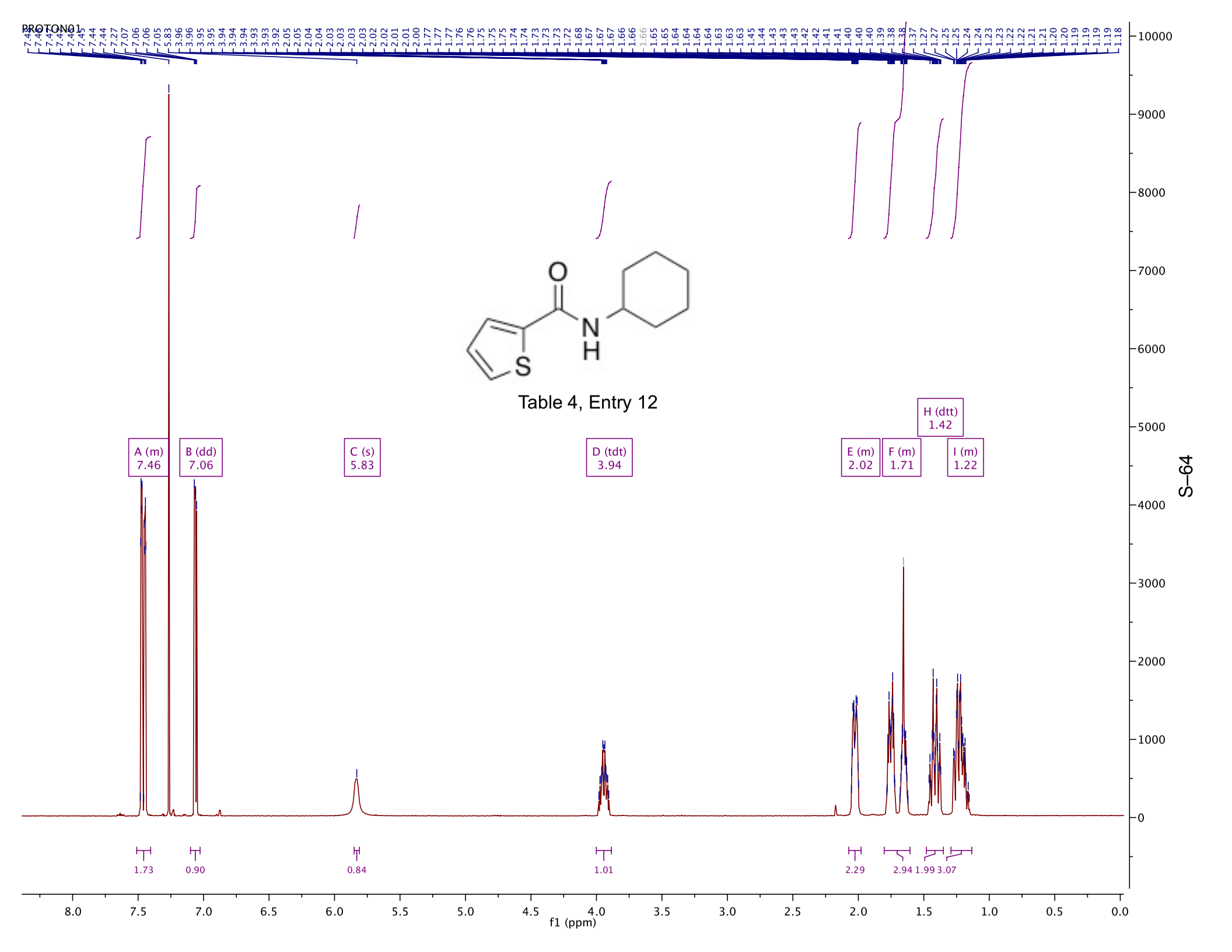

PROTON01
O
N
H
NC
Table 4, Entry 7
A (m)
7.85
B (m)
7.73
C (d)
6.01
D (tdt)
3.97
E (m)
2.03
G (m)
1.72
H (dtt)
1.43
I (dtdd)
1.23
1.93 1.85
1.04
0.99
2.37 2.89 2.02 2.91
f1 (ppm)

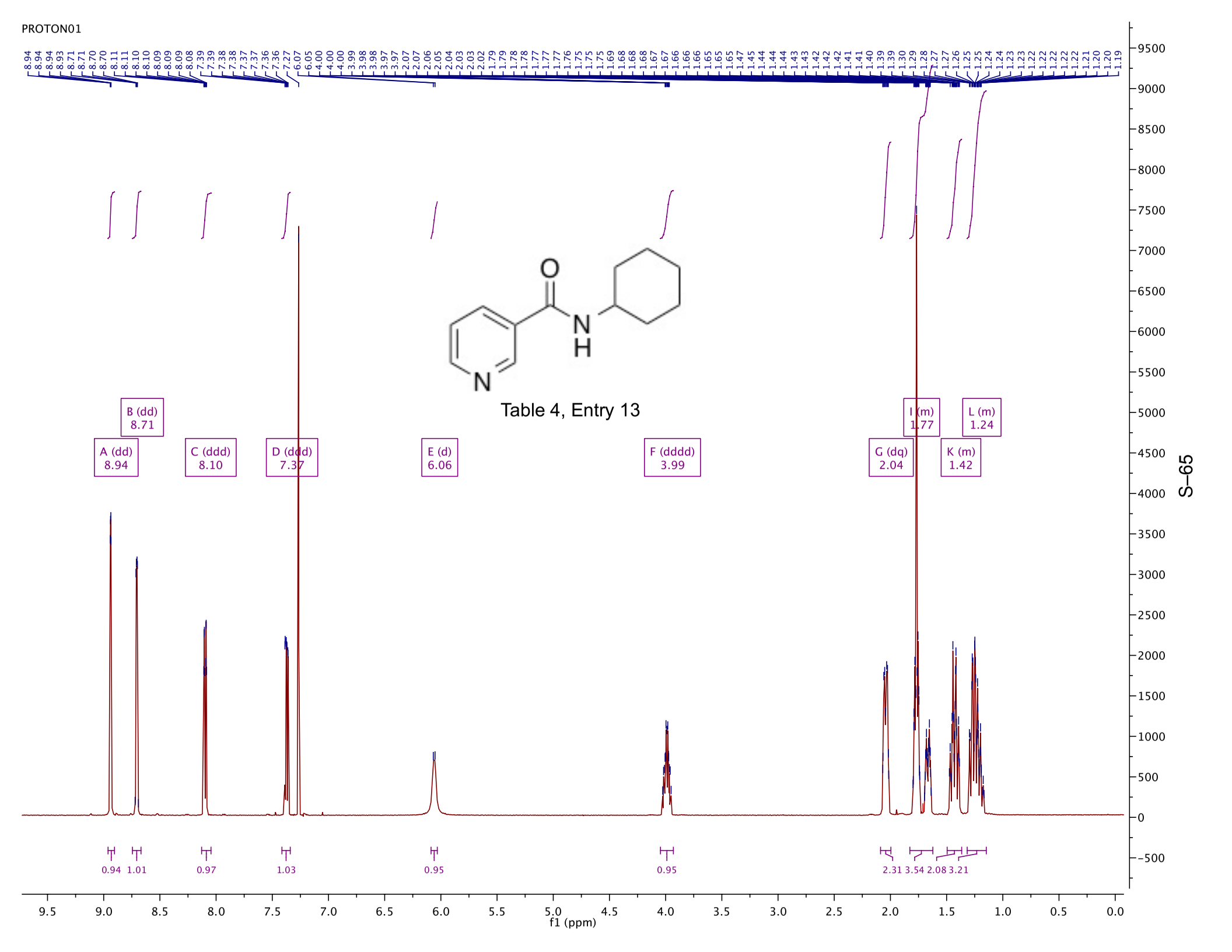

PROTON01
O
N
H
Table 4, Entry 8
B (dt) 8.26
C (m) 7.88
E (m) 7.55
F (d) 6.13
G (tdt) 4.05
H (dt) 2.09
J (m) 1.74
L (dtt) 1.46
M (m) 1.27
0.99
4.06
1.89
0.97
0.94
1.96
2.65
2.01
3.00
f1 (ppm)
S–60

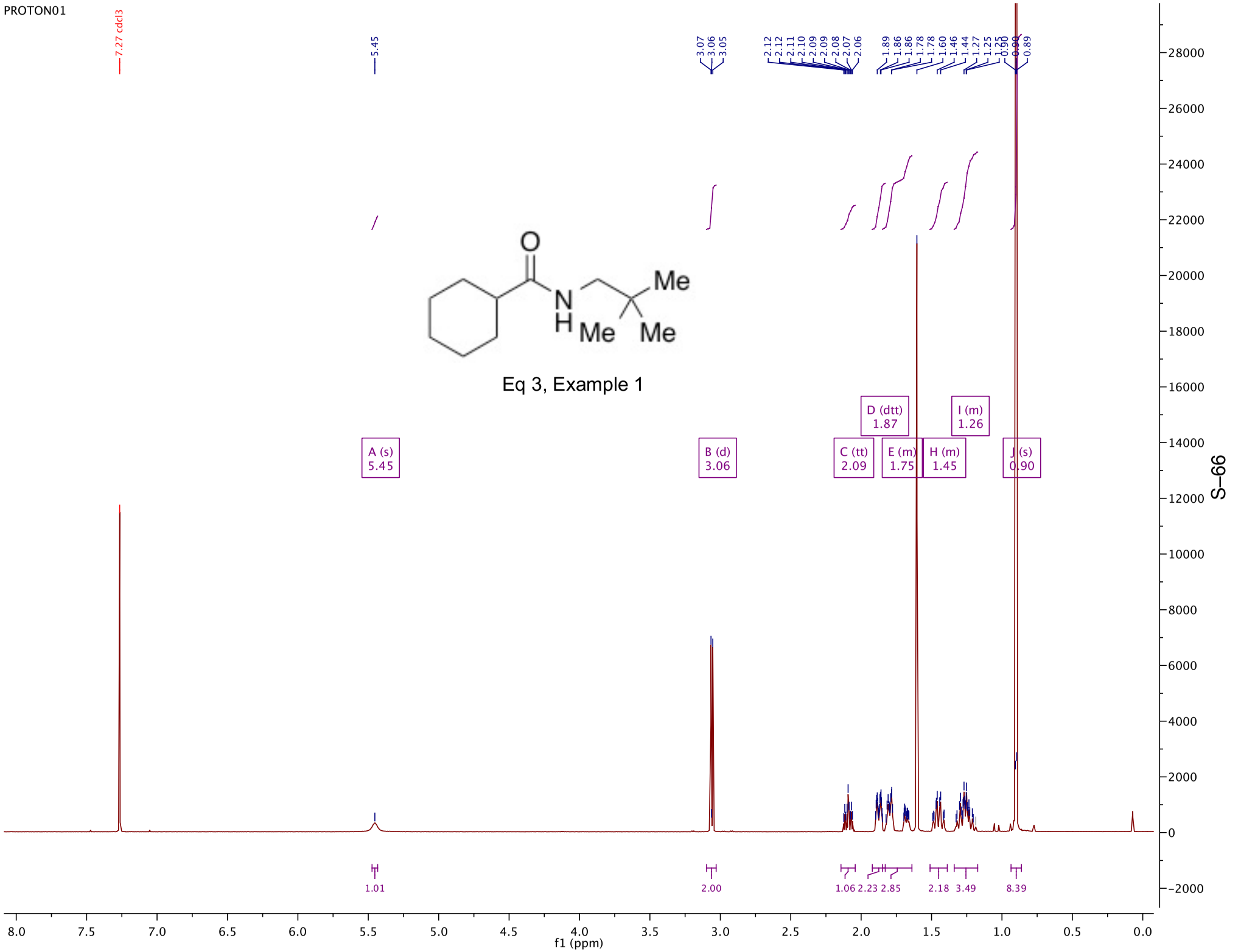

PROTON01
O
N
H
Table 4, Entry 9
A (m) 8.28
B (m) 7.89
C (m) 7.53
D (d) 5.87
E (tdt) 4.11
G (m) 2.12
J (m) 1.74
L (dtt) 1.47
M (m) 1.25
0.89
2.00
3.76
0.94
0.92
2.19
2.85
1.92
2.96
f1 (ppm)

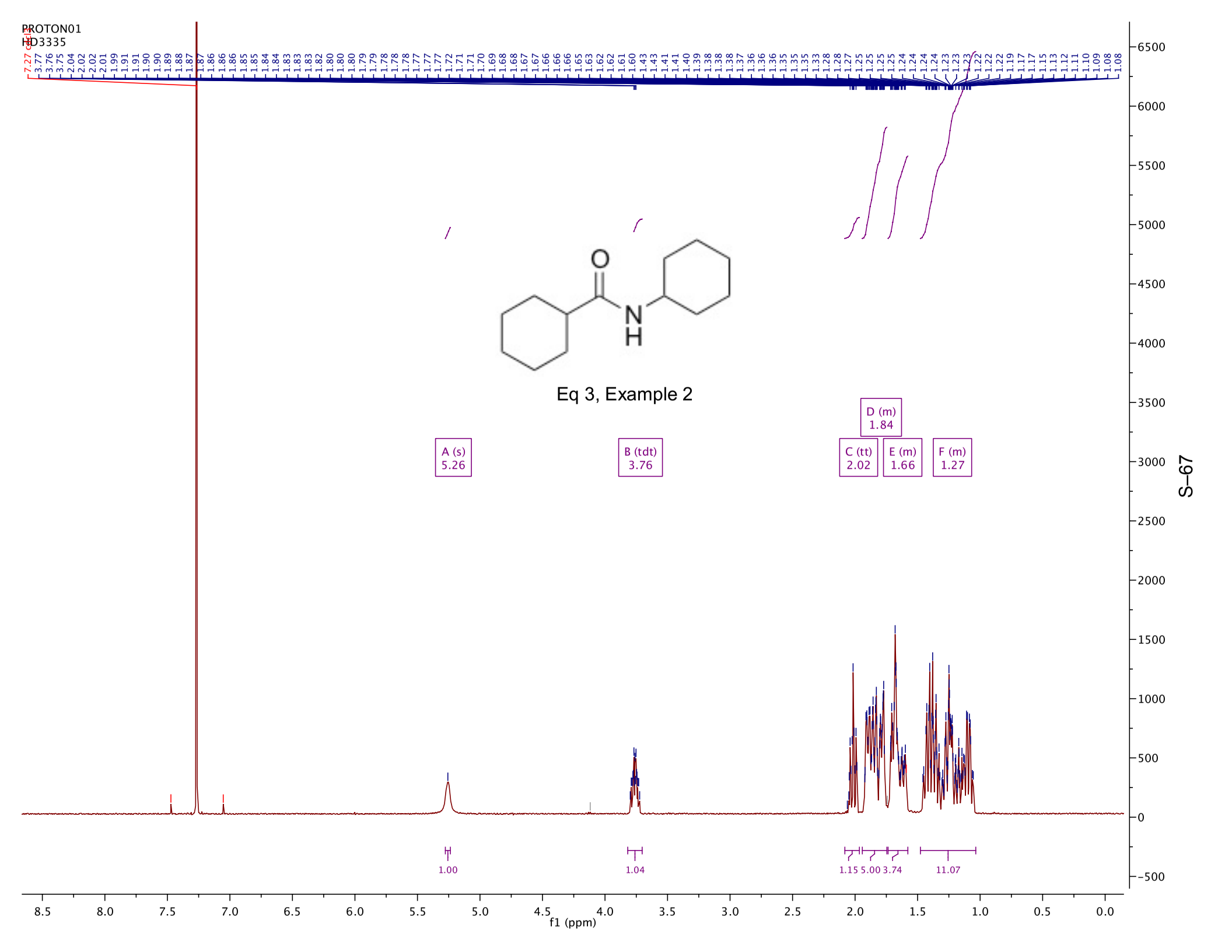

PROTON01
O
N
H
O
Table 4, Entry 10
B (dd) 7.42
D (dd) 7.09
E (dd) 6.49
F (m) 6.22
G (tdt) 3.94
I (m) 2.00
J (m) 1.70
L (dtt) 1.42
M (m) 1.24
0.83
0.84
1.00
0.92
0.97
2.27
3.49
2.11
3.10
f1 (ppm)

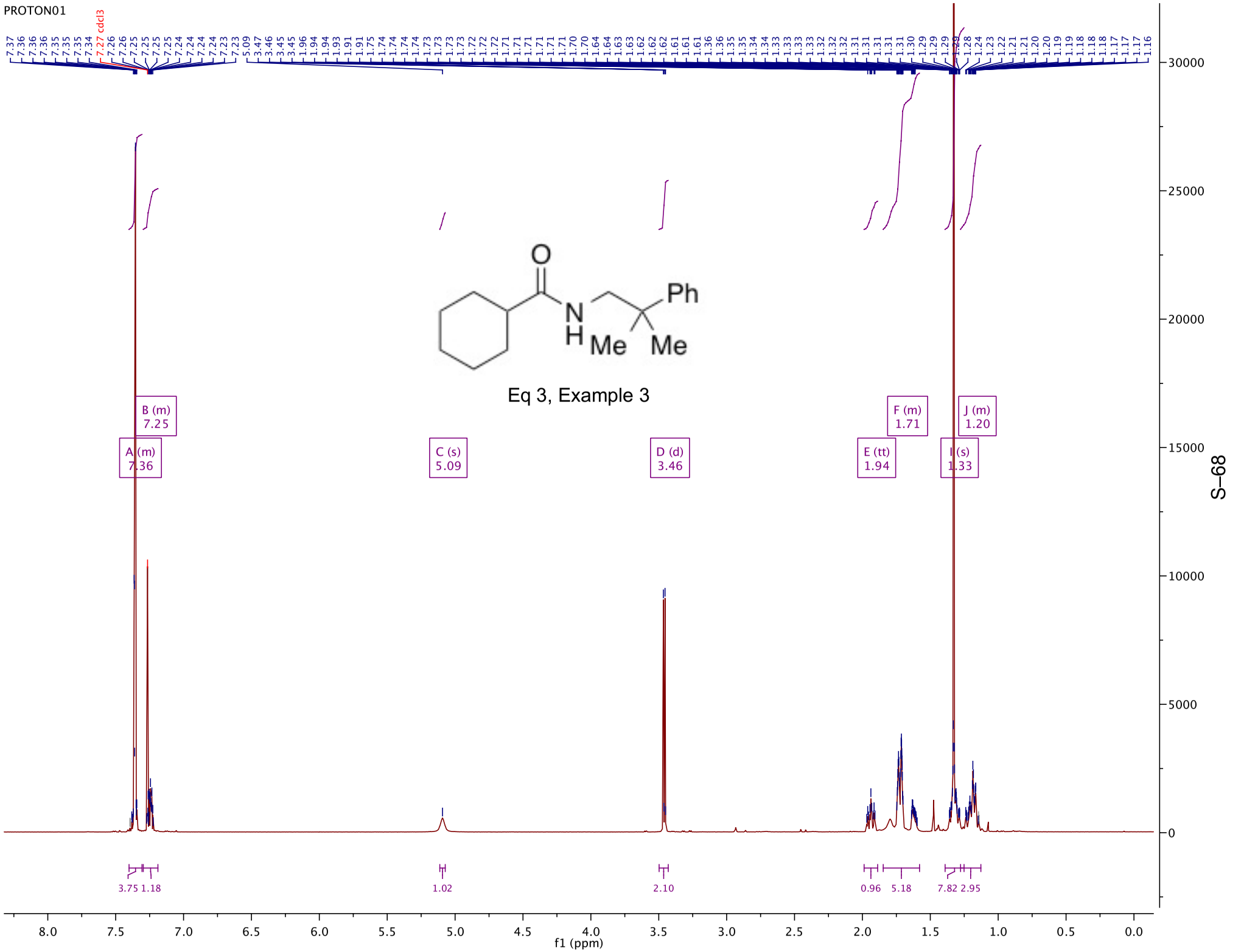

PROTON01
7.42 7.42 7.42 7.42 7.27 cdcl3 7.10 7.09 7.09 7.09
6.49 6.49 6.49 6.48
6.09 6.07
4.29 4.27 4.27 4.26 4.26 4.26 4.25 4.25 4.24 4.24 4.24 4.24 4.23 4.23 4.22 4.21 4.20
1.70 1.69 1.69 1.68 HDO 1.68 1.67 1.66 1.66 1.65 1.49 1.48 1.47 1.46 1.46 1.45 1.44 1.43 1.35 1.34 1.34 1.33 1.32 1.31 1.30 1.22 1.21 0.95 0.94 0.94 0.94 0.93 0.93 0.92 0.92 0.91
O
Me
Me
N
H
Me
O
Table 4, Entry 11
A (dd) 7.42
B (dd) 7.09
C (dd) 6.49
D (d) 6.08
E (m) 4.24
F (ddq) 1.68
G (ddd) 1.46
H (ddd) 1.33
I (d) 1.22
J (t) 0.94
0.83 0.85 0.97 0.94 0.98 1.27 1.10 1.06 2.98 5.94
f1 (ppm)
S–63

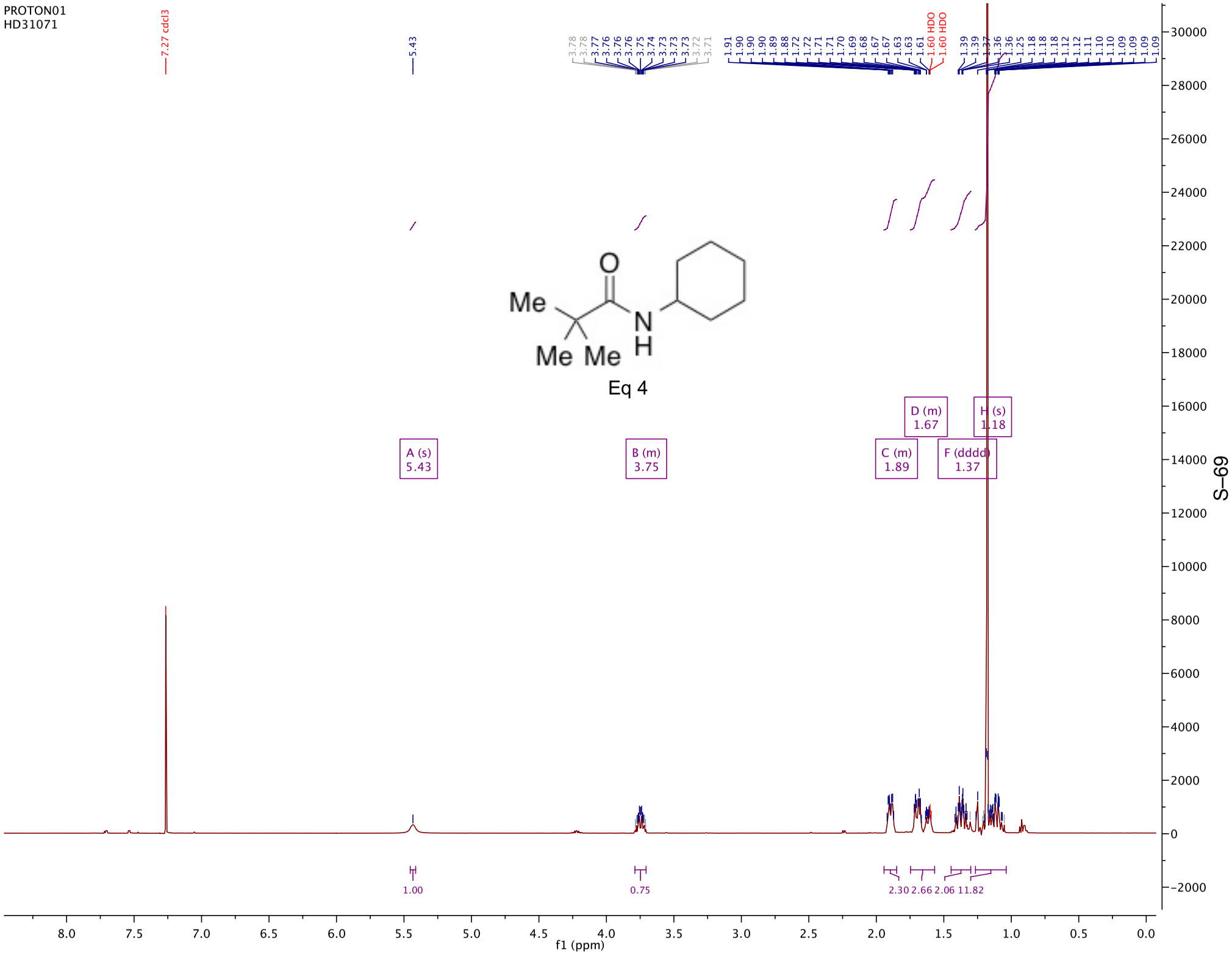

PROTON01
O
N
H
S
Table 4, Entry 12
A (m) 7.46
B (dd) 7.06
C (s) 5.83
D (tdt) 3.94
E (m) 2.02
F (m) 1.71
H (dtt) 1.42
I (m) 1.22
1.73
0.90
0.84
1.01
2.29
2.94
1.99
3.07
f1 (ppm)

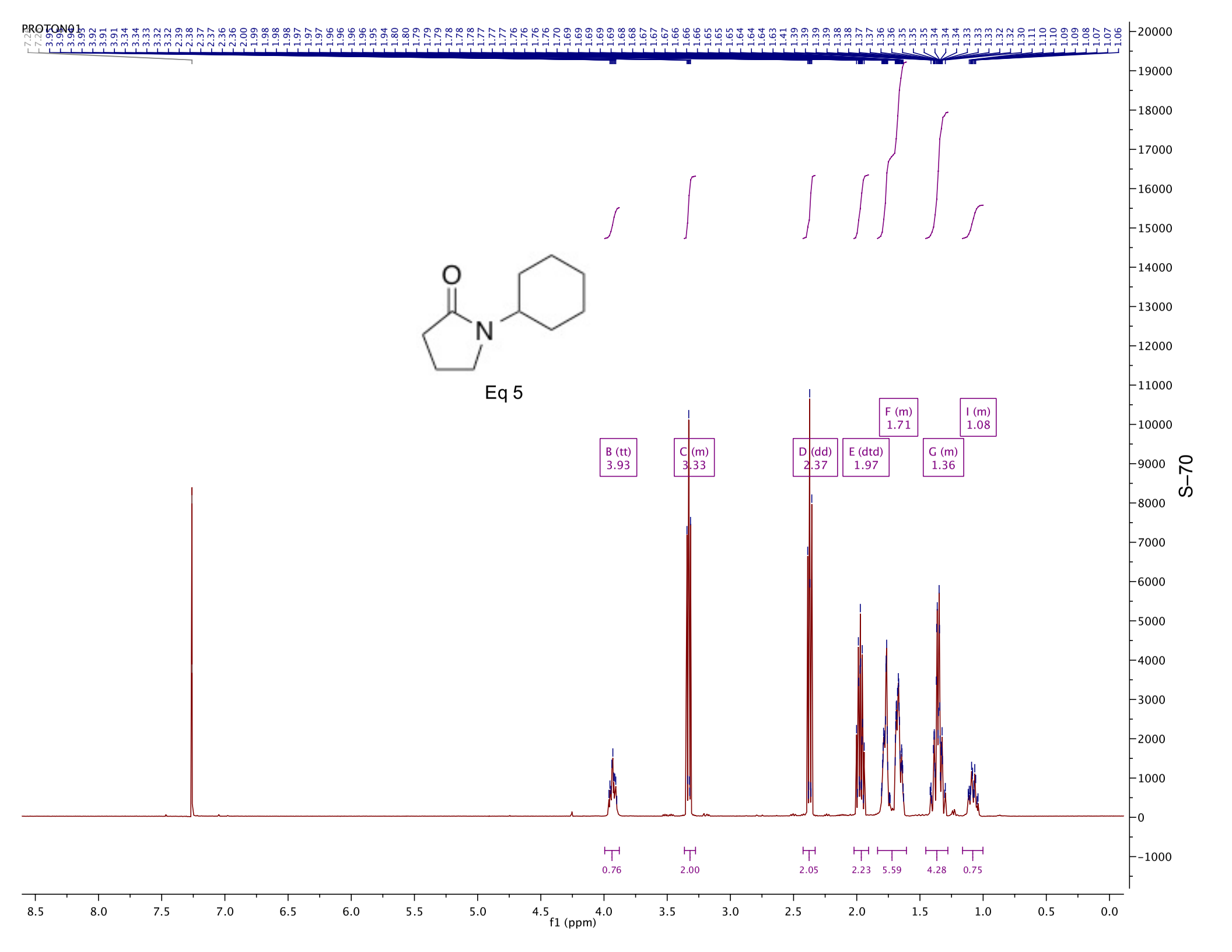

PROTON01
O
N
H
N
Table 4, Entry 13
A (dd) 8.94
B (dd) 8.71
C (ddd) 8.10
D (ddd) 7.37
E (d) 6.06
F (dddd) 3.99
G (dq) 2.04
I (m) 1.77
K (m) 1.42
L (m) 1.24
0.94 1.01 0.97 1.03 0.95 0.95 2.31 3.54 2.08 3.21
f1 (ppm)

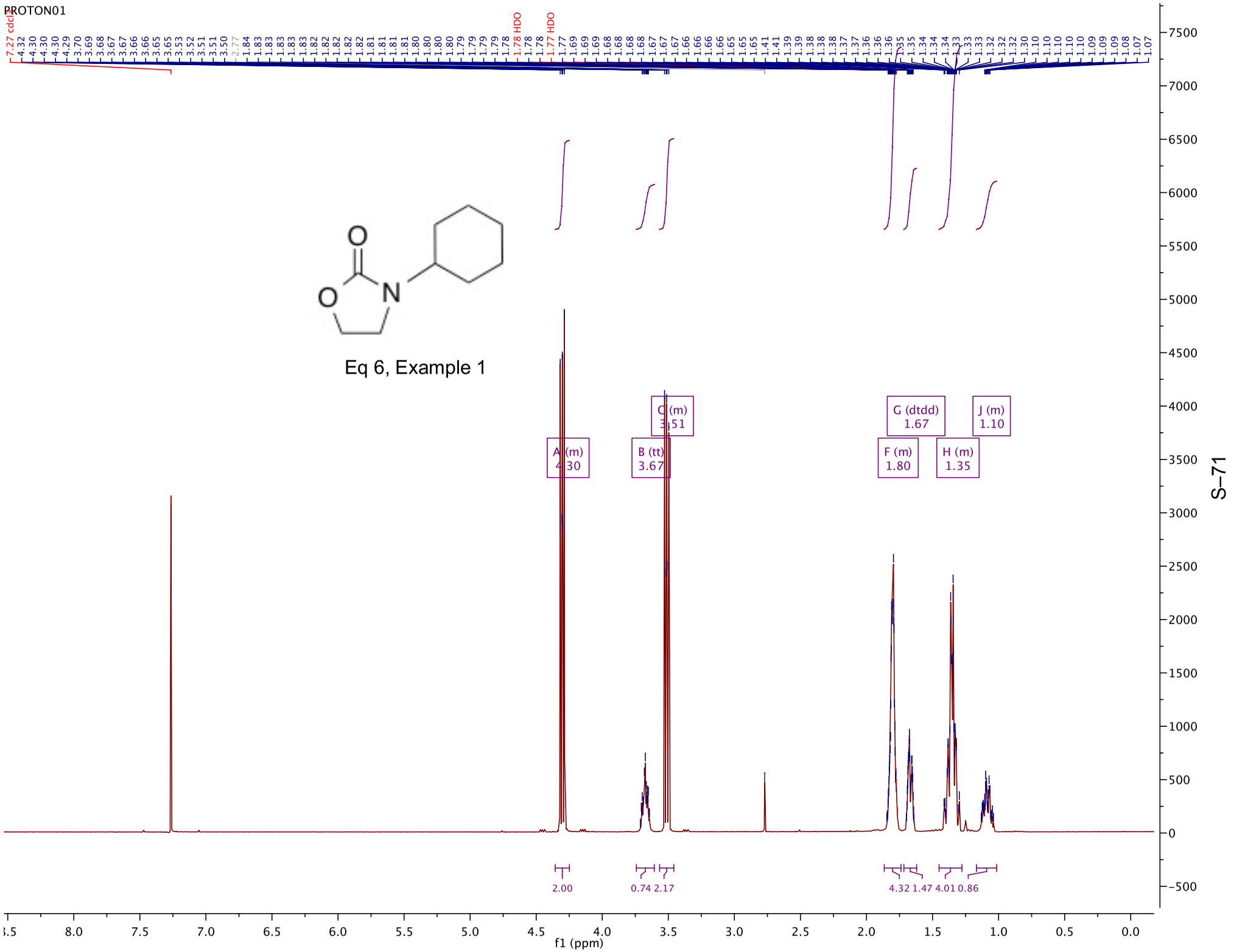

PROTON01
7.27 cdcl3
5.45
3.07
3.06
3.05
2.12
2.12
2.11
2.10
2.09
2.09
2.08
2.07
2.06
1.89
1.86
1.86
1.78
1.60
1.46
1.44
1.27
1.25
0.90
0.89
O
N
H
Me
Me
Me
Eq 3, Example 1
A (s)
5.45
B (d)
3.06
C (tt)
2.09
D (dtt)
1.87
E (m)
1.75
H (m)
1.45
I (m)
1.26
J (s)
0.90
1.01
2.00
1.06
2.23
2.85
2.18
3.49
8.39
f1 (ppm)
S–66

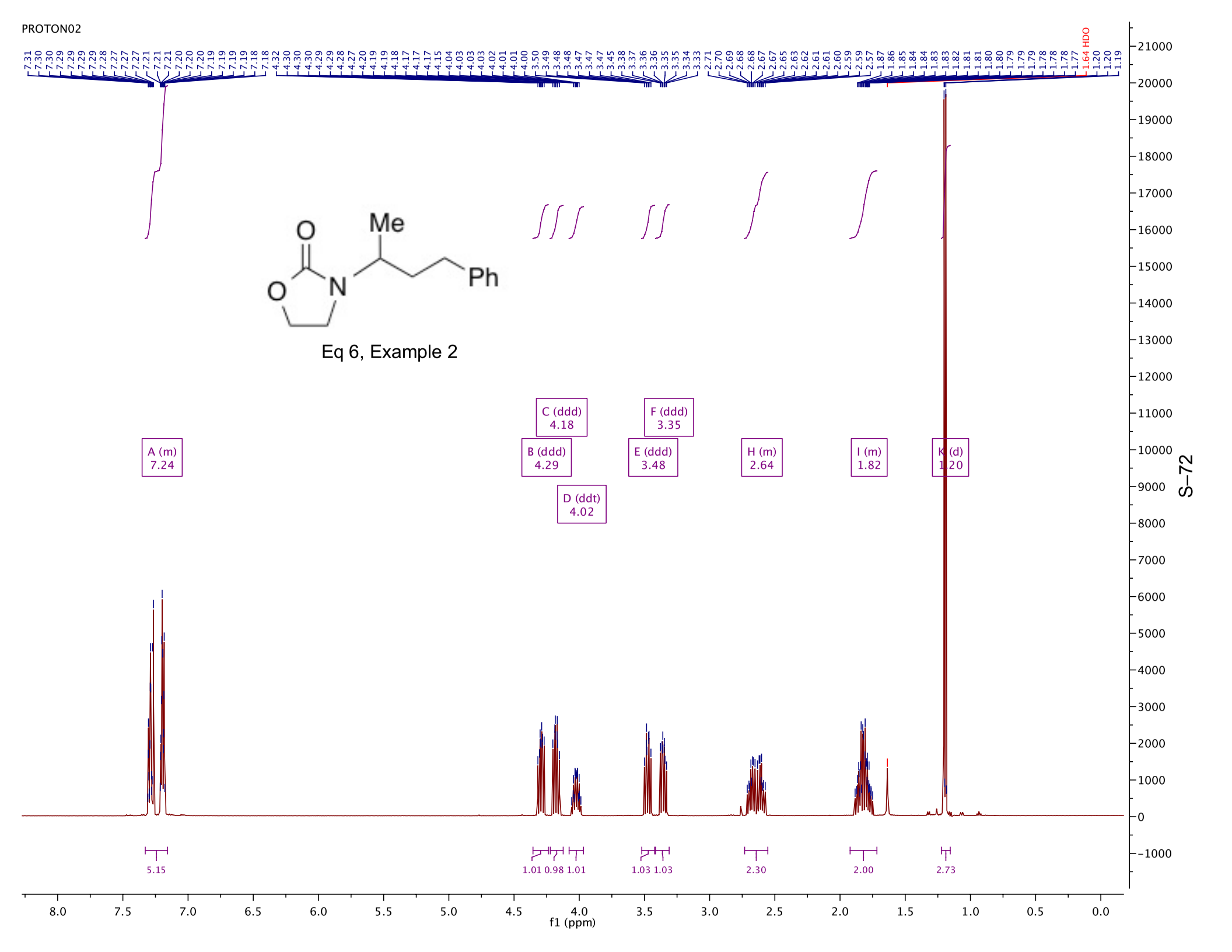

PROTON01
HD3335
O
N
H
Eq 3, Example 2
A (s)
5.26
B (tdt)
3.76
D (m)
1.84
C (tt)
2.02
E (m)
1.66
F (m)
1.27
1.00
1.04
1.15
5.00
3.74
11.07
f1 (ppm)

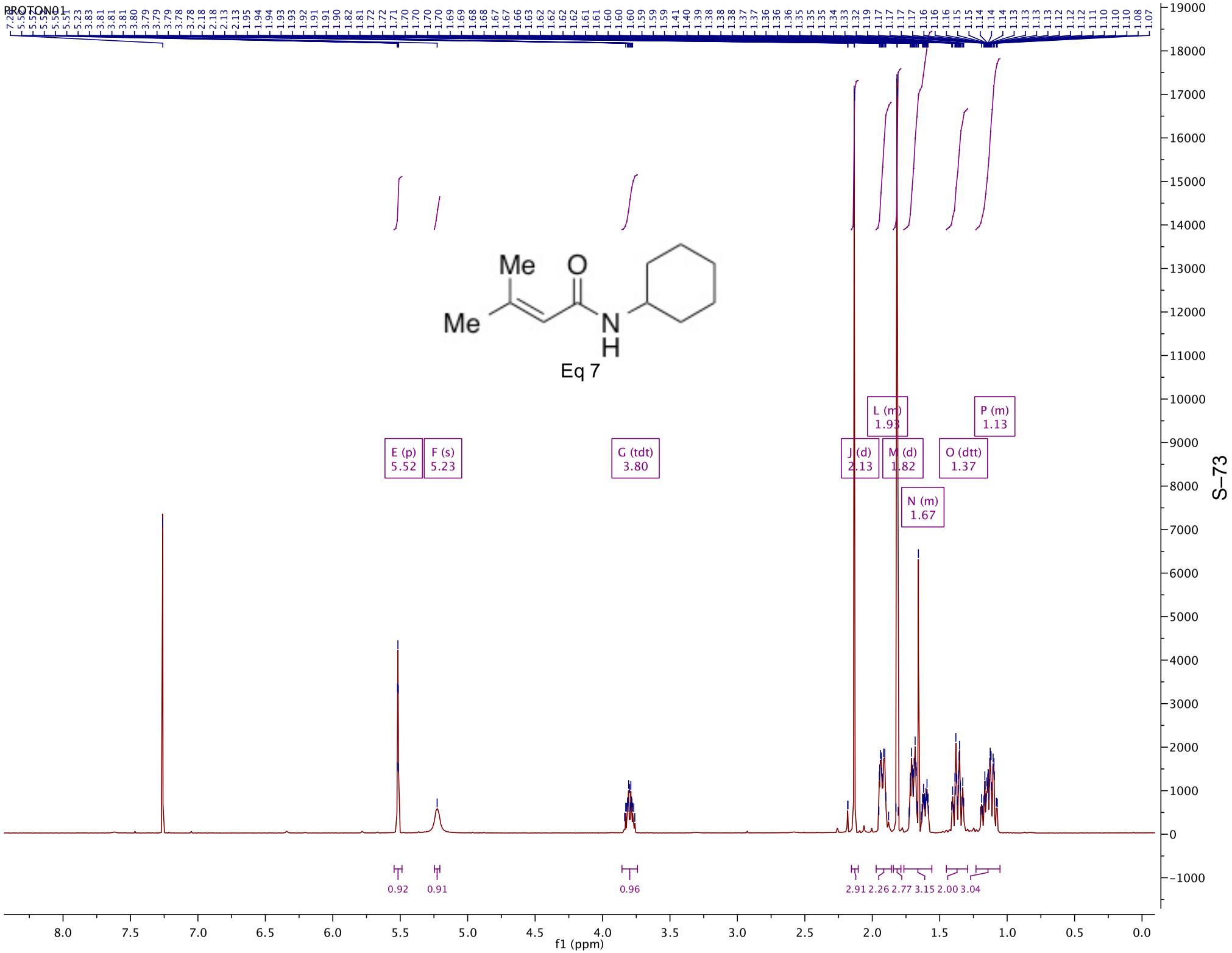

PROTON01
7.27 cdcl3
O
N
H
Ph
Me
Me
Eq 3, Example 3
A (m) 7.36
B (m) 7.25
C (s) 5.09
D (d) 3.46
E (tt) 1.94
F (m) 1.71
I (s) 1.33
J (m) 1.20
3.75 1.18
1.02
2.10
0.96 5.18
7.82 2.95
f1 (ppm)


PROTON01
HD31071
7.27 cdcl3
5.43
3.78 3.78 3.77 3.76 3.76 3.75 3.74 3.73 3.73 3.72 3.71
1.91 1.90 1.90 1.89 1.88 1.72 1.72 1.71 1.71 1.70 1.69 1.68 1.67 1.67 1.63 1.63 1.61
1.60 HDO
1.60 HDO
1.39 1.39 1.37 1.36 1.25 1.18 1.18 1.12 1.11 1.10 1.09 1.09 1.09 1.09
Me
O
N
H
Me Me
Eq 4
A (s) 5.43
B (m) 3.75
C (m) 1.89
D (m) 1.67
F (dddd) 1.37
H (s) 1.18
1.00
0.75
2.30 2.66 2.06 11.82
f1 (ppm)
S–69

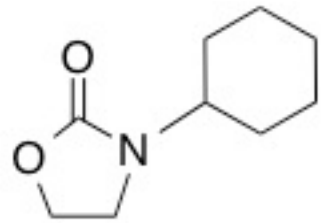

PROTON01
O
N
Eq 5
B (tt)
3.93
C (m)
3.33
D (dd)
2.37
E (dtd)
1.97
F (m)
1.71
G (m)
1.36
I (m)
1.08
0.76
2.00
2.05
2.23
5.59
4.28
0.75
f1 (ppm)
S–70


PROTON01
Eq 6, Example 1
A (m) 4.30
B (tt) 3.67
C (m) 3.51
F (m) 1.80
G (dtdd) 1.67
H (m) 1.35
J (m) 1.10
2.00
0.74 2.17
4.32 1.47 4.01 0.86
f1 (ppm)
S–71


PROTON02
O
Me
O
N
Ph
Eq 6, Example 2
A (m)
7.24
C (ddd)
4.18
B (ddd)
4.29
D (ddt)
4.02
F (ddd)
3.35
E (ddd)
3.48
H (m)
2.64
I (m)
1.82
K (d)
1.20
5.15
1.01 0.98 1.01
1.03 1.03
2.30
2.00
2.73
f1 (ppm)
S–72


PROTON01
Me
O
Me
N
H
Eq 7
E (p)
5.52
F (s)
5.23
G (tdt)
3.80
J (d)
2.13
M (d)
1.82
L (m)
1.93
O (dtt)
1.37
P (m)
1.13
N (m)
1.67
0.92
0.91
0.96
2.91
2.26
2.77
3.15
2.00
3.04
f1 (ppm)
S–73

PROTON01
HD31057

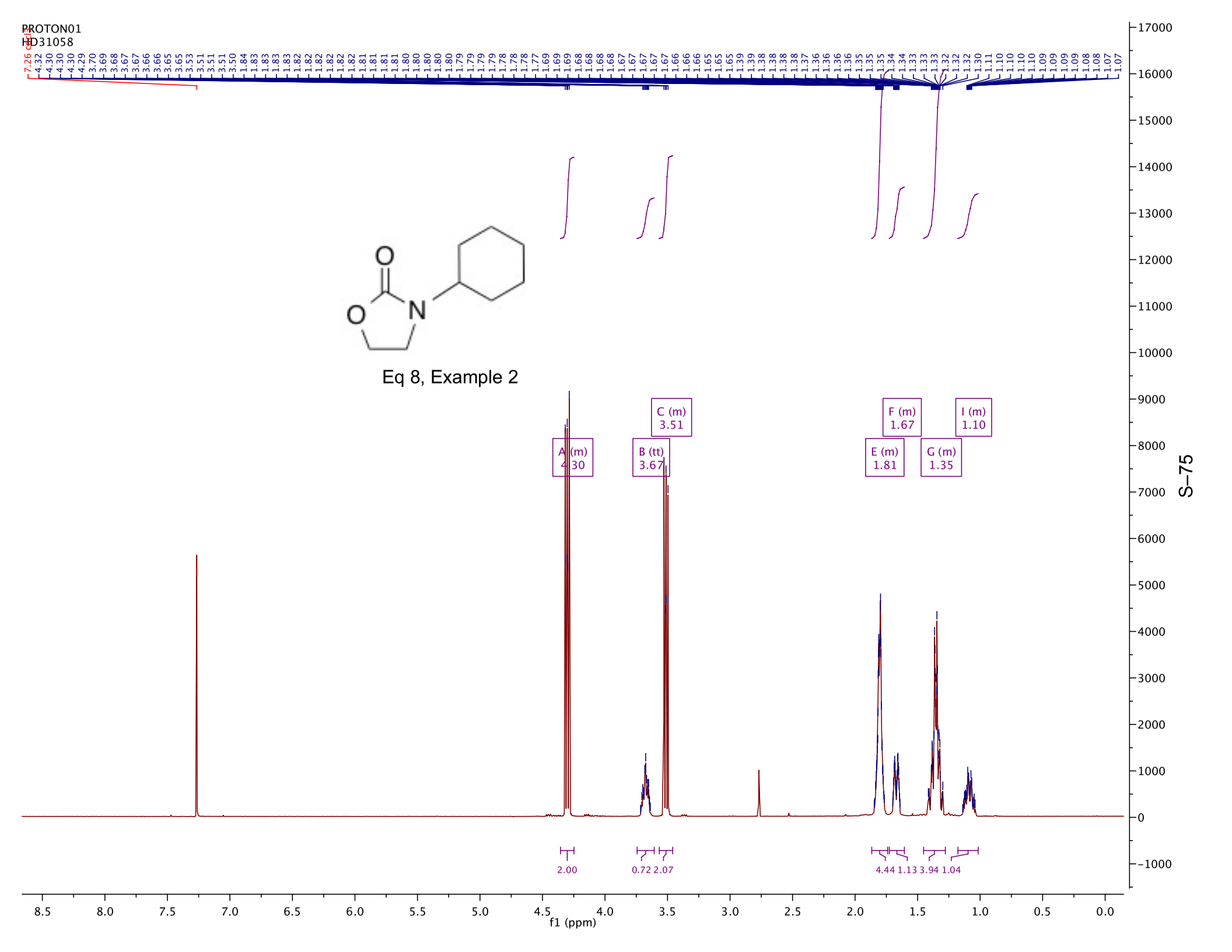


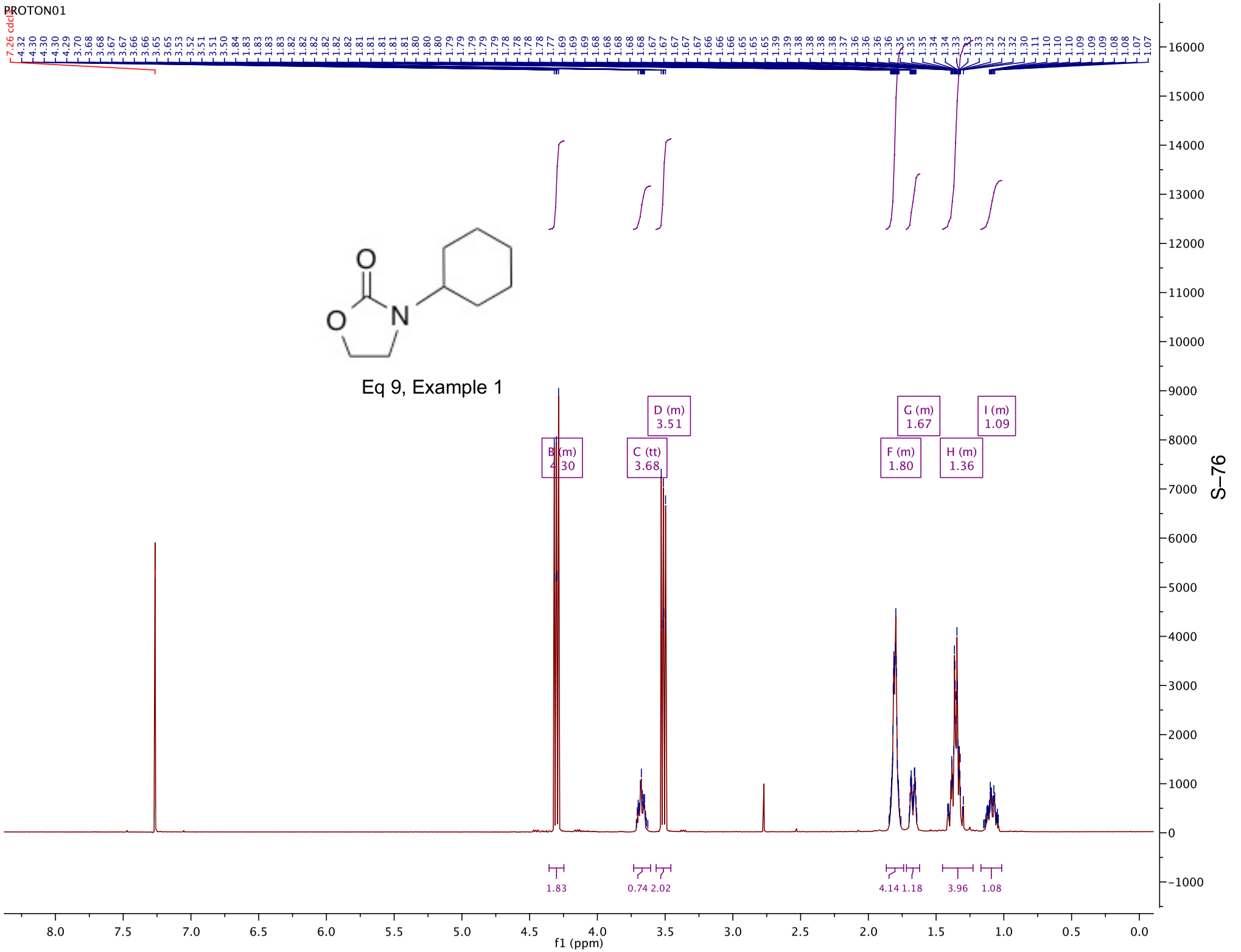
Eq 8, Example 1

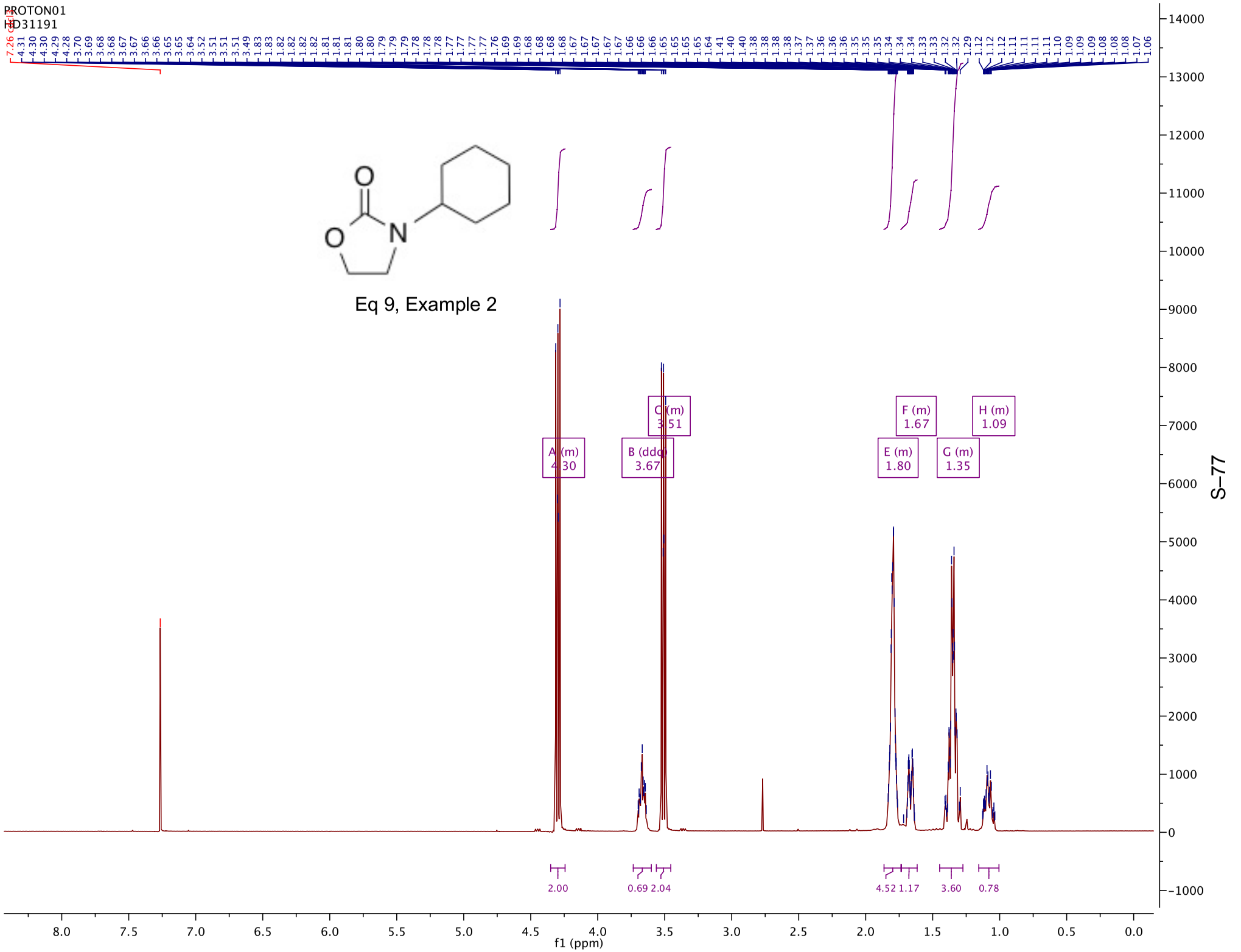
B (m) 4.30
C (tt) 3.68
D (m) 3.51
F (m) 1.80
G (m) 1.67
H (m) 1.36
I (m) 1.09

2.00 0.81 2.21 4.53 1.30 4.33 1.18

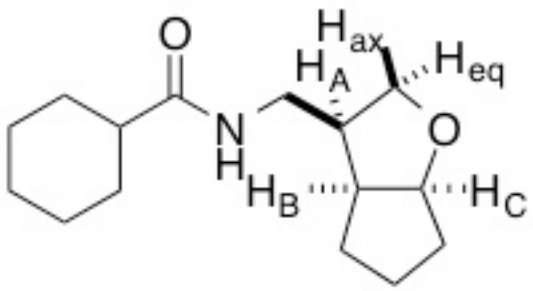
f1 (ppm)


PROTON01
HD31058
Eq 8, Example 2
A (m) 4.30
B (tt) 3.67
C (m) 3.51
E (m) 1.81
F (m) 1.67
G (m) 1.35
I (m) 1.10
2.00
0.72 2.07
4.44 1.13 3.94 1.04
f1 (ppm)
S–75


PROTON01
7.26 cdcl3
O
O
N
Eq 9, Example 1
B (m)
4.30
C (tt)
3.68
D (m)
3.51
F (m)
1.80
G (m)
1.67
H (m)
1.36
I (m)
1.09
1.83
0.74 2.02
4.14 1.18
3.96
1.08
f1 (ppm)
S–76


PROTON01
HD31191
O
O
N
Eq 9, Example 2
A (m)
4.30
B (ddd)
3.67
C (m)
3.51
E (m)
1.80
F (m)
1.67
G (m)
1.35
H (m)
1.09
2.00
0.69 2.04
4.52 1.17
3.60
0.78
f1 (ppm)
S–77

PROTON02
SB-I-271-major

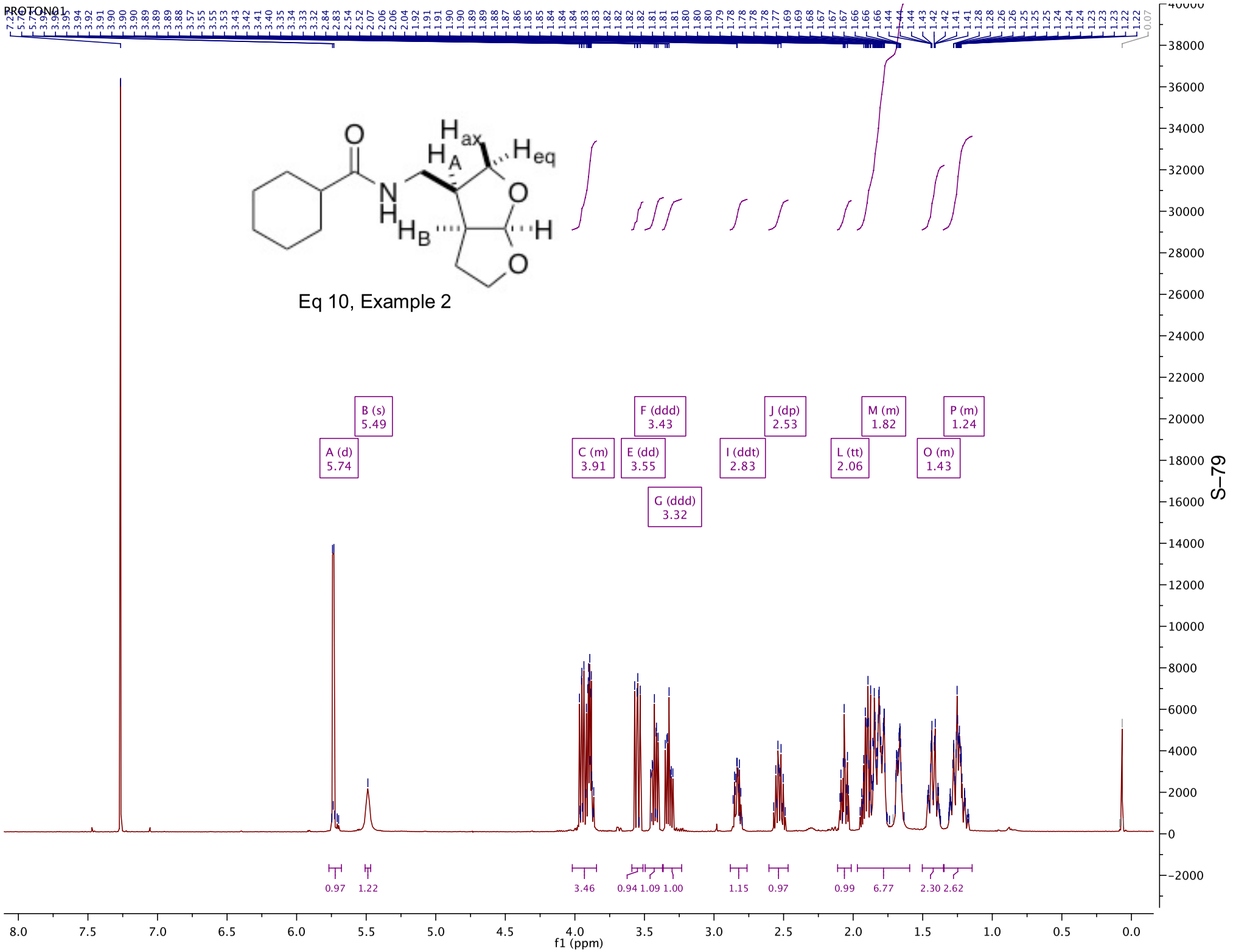


Eq 10, Example 1

D (d) 5.55
E (td) 4.51
G (dd) 3.84
H (m) 3.45
I (m) 3.32
J (m) 2.53
N (tt) 2.05
O (m) 1.74
P (m) 1.49
Q (m) 1.24

0.98 1.04 0.96 0.90 2.05 1.85 0.99 8.33 4.91 3.19

f1 (ppm)


PROTON01
Eq 10, Example 2
A (d) 5.74
B (s) 5.49
C (m) 3.91
E (dd) 3.55
F (ddd) 3.43
G (ddd) 3.32
I (ddt) 2.83
J (dp) 2.53
L (tt) 2.06
M (m) 1.82
O (m) 1.43
P (m) 1.24
0.97 1.22
3.46
0.94 1.09 1.00
1.15
0.97
0.99
6.77
2.30 2.62
f1 (ppm)

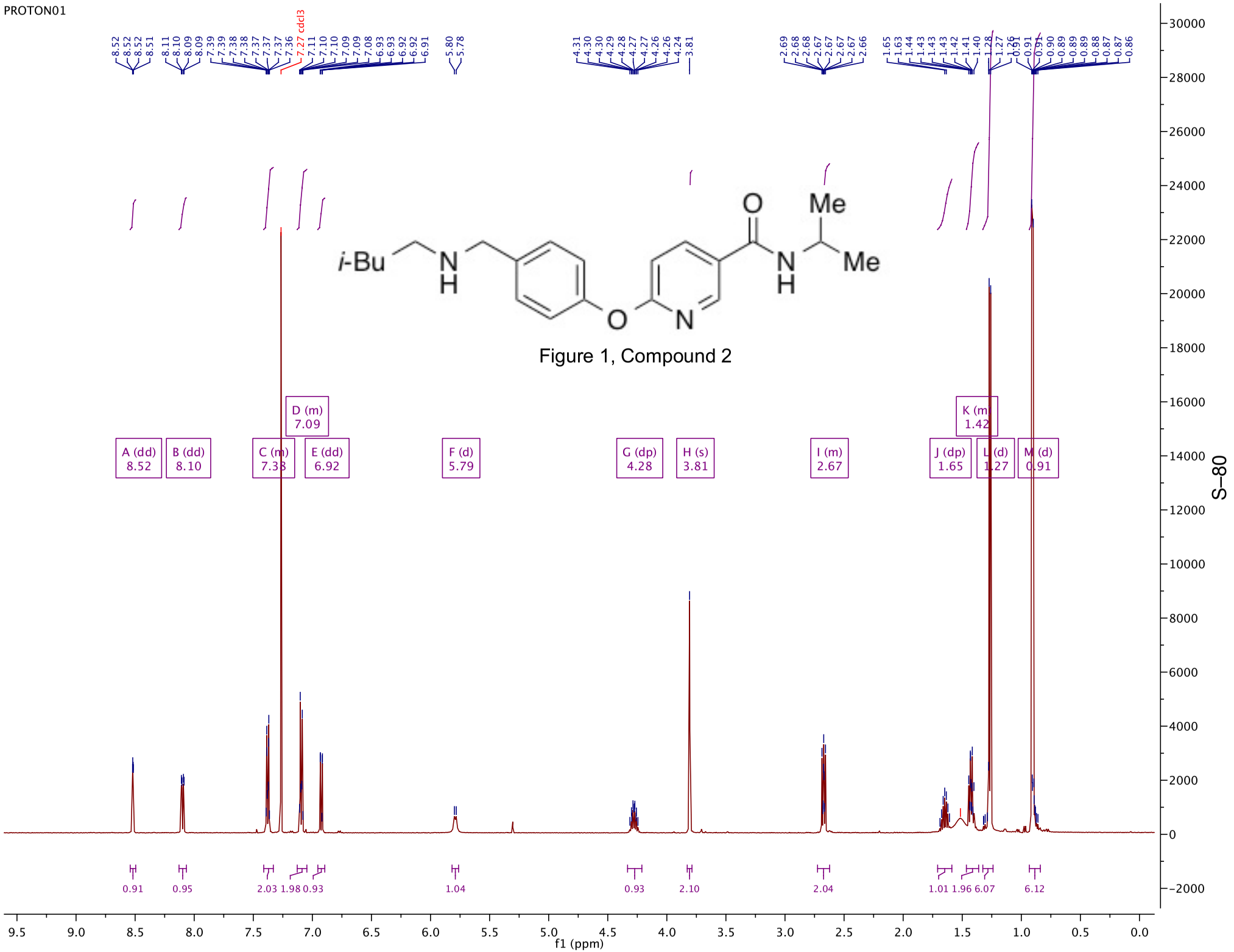


Figure 1, Compound 2